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Guidance for the Reregistration of Pesticide Products Containing Metiram the Active Ingredient

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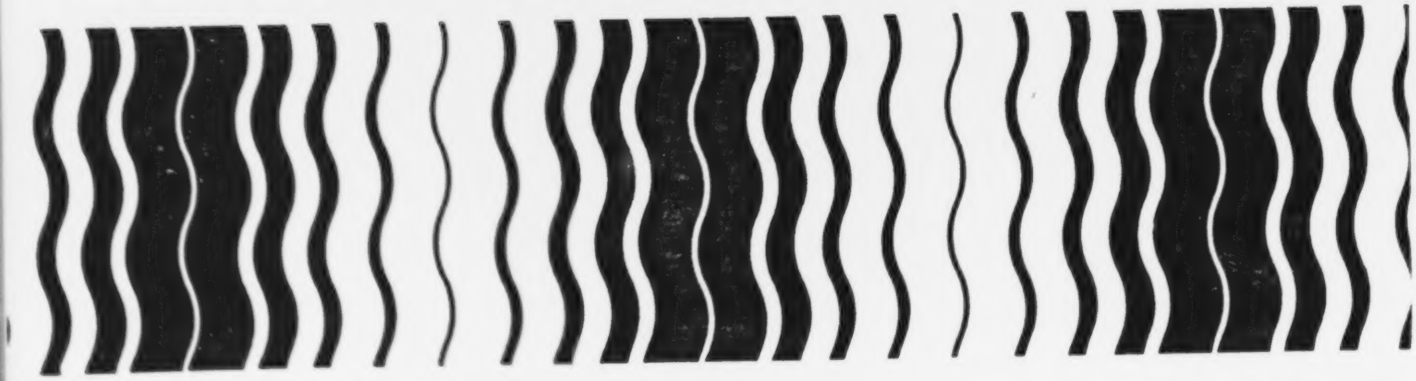
EPA

Guidance for the Reregistration of Pesticide Products Containing METIRAM as the Active Ingredient



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This document contains information regarding the reregistration of pesticide products containing the subject active ingredient. The document includes how to register under a registration standard, regulatory position and rationale, and summaries of data requirements and data gaps. Also included is a bibliography containing citations of all studies reviewed by EPA in arriving at the positions and conclusions contained in the standard.

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GUIDANCE FOR THE REREGISTRATION OF PESTICIDE PRODUCTS

CONTAINING

METIRAM
AS THE ACTIVE INGREDIENT

CASE NUMBER 0644

CAS (Docket) Number 9006-42-2

EPA CHEMICAL CODE 014601

OCTOBER 1988

ENVIRONMENTAL PROTECTION AGENCY

OFFICE OF PESTICIDE PROGRAMS

WASHINGTON, D.C. 20460

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EPA Form 8580-1	FIFRA §3(c)(2)(B) Summary Sheet
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GLOSSARY OF TERMS AND ABBREVIATIONS

The following terms are used throughout this Registration Standard and are defined here for the convenience of the reader.

ADI: (Acceptable Daily Intake) An acceptable daily intake of pesticide residue based on a complete data base.

ai: Active ingredient

CAS: Chemical Abstract Service (number)

EEC: (Estimated Environmental Concentration) Estimated pesticide concentration in the environment (terrestrial or aquatic ecosystem).

EP: End-use Product

EPA: The Environmental Protection Agency, also "the Agency"

FIFRA: The Federal Insecticide, Fungicide, and Rodenticide Act

HDT: Highest dose tested

LC_{50}: (median lethal concentration): a statistically derived concentration of a substance that can be expected to cause death in 50 percent of test animals, expressed as weight or volume of test substance per volume of air or water or per weight of feed (e.g., mg/L or ppm).

LD_{50}: (median lethal dose): a statistically derived single dose that can be expected to cause death in 50 percent of animals when administered by the route indicated, expressed as weight of substance per unit weight of test animal (e.g., mg/kg).

LEL: Lowest Effect Level

MOS: Margin of Safety -

MPI: Maximum Permissible Intake

MRID: Master Record Identification (number)--EPA's system of tracking studies used in support of registrations

MP: Manufacturing-use product

NPDES: National Pollution Discharge Elimination System

NOEL: No Observed Effect Level--the maximum dose used in a test which produces no observed adverse effects.

OPP: The Office of Pesticide Programs (EPA)

OM: Organic matter (used to describe soils)

ppm: Parts per million

PADI: (Provisional Acceptable Daily Intake) An acceptable daily intake of pesticide residue based on a limited data base.

PAI: Pure active ingredient

Technical: Active ingredient as manufactured

TMRC: (Theoretical Maximum Residue Contribution)

I. INTRODUCTION

EPA has established the Registration Standards program in order to provide an orderly mechanism by which pesticide products containing the same active ingredient can be reviewed and standards set for compliance with FIFRA. The standards are applicable to reregistration and future applications for registration of products containing the same active ingredient. Each registrant of a product containing an active ingredient subject to this Standard who wishes to continue to sell or distribute that product must bring his product and labeling into compliance with FIFRA, as instructed by this Standard.

The Registration Standards program involves a thorough review of the scientific data base underlying a pesticide's registration. The purpose of the Agency's review is to reassess the potential hazards arising from the currently registered uses of the pesticide; to determine the need for additional data on health and environmental effects; and to determine whether the pesticide meets the "no unreasonable adverse effects" criteria of FIFRA. In its review EPA identifies:

1. Studies that are acceptable to support the data requirements for the currently registered uses of the pesticide.

2. Additional studies necessary to support continued registration. The additional studies may not have been required when the product was initially registered or may be needed to replace studies that are now considered inadequate.

3. Labeling revisions needed to ensure that the product is not misbranded and that the labeling is adequate to protect man and the environment.

The detailed scientific review and use index which are not contained in this document, but is available upon request[1], focuses on the pesticide active ingredient. The scientific review primarily discusses the Agency's evaluation of and conclusions from available data in its files pertaining to the pesticide active ingredient. However, during the review of these data the Agency is also looking for potential hazards that may be associated with the end use products that contain the active ingredient. The Agency will apply the provisions of this Registration Standard to end use products if necessary to protect man and the environment.

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[1] The scientific reviews and use index are available from the National Technical Information Service, 5285 Port Royal Road, Springfield, Va. 22161 or from the Order Desk (703) 487-4650.

EPA's reassessment results in the development of a regulatory position, contained in this Registration Standard, on the pesticide and each of its registered uses. See Section IV - Regulatory Position and Rationale. Based on its regulatory position, the Agency may prescribe a variety of steps to be taken by registrants to maintain their registrations in compliance with FIFRA. These steps may include:

1. Submission of data in support of product registration;

2. Modification of product labels;

3. Modifications to the manufacturing process of the pesticide to reduce the levels of impurities or contaminants;

4. Restriction of the use of the pesticide to certified applicators or other specially trained individuals;

5. Modification of uses or formulation types; or

6. Specification of packaging limitations.

Failure to comply with the data submission requirements may result in the issuance of a Notice of Intent to Suspend. Failure to comply with the other requirements in this Standard may result is the issuance of a Notice of Intent to Cancel.

In addition, in cases in which hazards to man or the environment are identified, the Agency may initiate a special review of the pesticide in accordance with 40 CFR Part 154 to examine in depth the risks and benefits of use of the pesticide. If the Agency determines that the risks of the pesticide's use outweigh the benefits of use, the Agency may propose additional regulatory actions, such as cancellation of uses of the pesticide which have been determined to cause unreasonable adverse effects on the environment.

EPA has authority under the Data Call-In (DCI) provisions of FIFRA sec. 3(c)(2)(B) to require that registrants submit data to answer our questions regarding the chemical, toxicological, and environmental characteristics and fate of a pesticide. This Registration Standard lists the data EPA believes are necessary to resolve our concerns about this pesticide. These data are listed in the Tables A, and B in Appendix I. Failure to comply with the DCI requirements enumerated in this Registration Standard may result in issuance by EPA of a Notice of Intent to Suspend the affected product registrations.

Registrants are reminded that FIFRA sec. 6(a)(2) requires them to submit factual information concerning possible unreasonable adverse effects of a pesticide at any time that they become aware of such information. Registrants must notify the Agency of any information, including interim or preliminary results of studies, if that information suggests possible adverse effects on man or the environment. This requirement is independent of the specific time requirements imposed by EPA for submission of completed studies called in by the Agency and continues as long as the products are registered under FIFRA.

II. CHEMICAL(S) COVERED BY THIS STANDARD

A. Description of chemical(s)

The following chemical(s) are covered by this Registration Standard:

Common name: Metiram

Chemical name: Mixture of 5.2 Parts by Weight (83.9%) of ammoniates of [ethylenebis(dithiocarbamate)]zinc with 1 part by weight (16.1%) ethylenebis[dithiocarbamic acid], bimolecular and trimolecular cyclic anhydrosulfides and disulfides

CAS Number: 9006-42-2

OPP (Shaughnessy) Numbers: 014601

Empirical Formula: $C_{16}H_{33}N_{11}S_{16}Zn_3$

Trade names: Polyram®, Polram-Comi®, Carbatene® and Zinc Metiram®

Description of physical characteristics of chemical
Color: Yellow
Melting Point: Approximately 140°C

B. Use Profile

Type of Pesticide: Fungicide (with minor insecticidal value).

Pests Controlled (in general): Foliar fungal diseases of selected fruit, nut, vegetable, field and ornamental crops.

Registered Uses: Terrestrial food crop uses on apples, asparagus, celery, corn (sweet), cotton, cucumber, peanuts, pecans, potatoes (including seed pieces), sugar beets, and tomato; Terrestrial nonfood crop uses on tobacco (field and transplants) and roses.

Predominant Use(s): Apple foliage and potato foliage and seed piece treatment

Mode of Activity: Inhibition of certain fungal enzyme systems

Formulation Types Registered:
Formulating intermediate - 80% percent active ingredient
End-use products - dusts, wettable powders

Method(s) of Application: All formulations may be applied by aerial equipment and ground equipment except the single active ingredient (3.5%) and 10% formulations used as seed piece treatments.

Application Rates - Terrestrial Food Crop: 0.3-6.4 lb ai/A
Terrestrial Nonfood Crop: 1.2-2.4 lb ai/A

C. Background

Metiram is one of six chemicals classified as ethylene bisdithiocarbamate (EBDC) fungicides. These broad spectrum fungicides are used to prevent crop damage by fungi and to protect harvested products from deterioration. The chemical structure of metiram and the other EBDC's (amobam, maneb, nabam, mancozeb, and zineb) and their metabolite, ethylenethiourea (ETU) are depicted in Figure 1.

The chemistry of the EBDC's is complicated by their instability and their propensity to form polymers. The solubilities of several of the EBDC's in water and other solvents vary from insoluble to completely soluble. The EBDC's are generally unstable in the presence of moisture and oxygen, as well as in biological systems. A common contaminant, degradation product, and metabolite of all EBDC's is ETU, an odorless white crystalline solid that is soluble in water but insoluble in common organic solvents. EBDC residues, in or on foods, are known to convert readily to ETU during commercial processing or home cooking.

In 1977, the Agency initiated a Special Review (formerly referred to as Rebuttable Presumption Against Registration [RPAR]) of the EBDC's. The Special Review process is designed to help the Agency determine whether to initiate procedures to cancel, deny or reclassify registration of a pesticide product because uses of that product may cause unreasonable adverse effects on the environment, in accordance with sections 3(c)(6) and 6 of FIFRA. This process is set forth in 40 CFR 154, which describes various risk criteria and provides that a Special Review may arise if the Agency determines that any of these criteria have been met.

The EBDC Special Review was based on the presumption that the EBDC's and the metabolite, ETU, posed three kinds of risk to human health or the environment: oncogenicity, teratogenicity, and acute toxicity to aquatic organisms. Three additional areas of concern were also identified: thyroid toxicity, mutagenicity, and skin sensitization. Skin sensitization was subsequently determined not to meet a Special Review criterion.

The Agency evaluated these potential risks in depth, taking into account uncertainties associated with the risk estimates, considering the significant benefits of the EBDC's and weighing various regulatory options. In 1982, the Agency issued its Decision Document on all EBDC's reporting on the results of the evaluation. This evaluation resulted in the following conclusions.

1. The potential risk of acute toxicity to aquatic organisms resulting from use of mancozeb on commercially grown wild rice would be mitigated through present cultivating practices and the addition of a statement to the label warning users of a hazard to fish.

2. Potential risks of teratogenicity and thyroid toxicity to commercial and agricultural applicators would be adequately reduced by requiring protective clothing.

3. Potential dietary exposure resulting from consumption of home grown produce could be reduced by highlighting preharvest intervals on labels of noncommercial (home use) products used by home gardeners.

4. The issues of whether EBDC's or ETU pose a potential risk of oncogenicity, mutagenicity, teratogenicity, and thyroid effects to man were subject to many uncertainties. Available data on oncogenicity and mutagenicity were not adequate to resolve key scientific issues such as the mechanism of action of EBDC's and ETU. Additional data on the EBDC's and ETU were needed for the Agency to determine their mutagenic potential and to assess human exposure and oncogenic risk. Some data would be required at termination of the Special Review while further data needs, with particular emphasis on chronic studies, dietary residues and exposure, would be identified during a later reregistration review. Data needs identified at that time included:

    a. Metabolism studies designed to define the *in vivo* conversion of the various EBDC's to ETU and other metabolites.

    b. Dermal absorption studies designed to demonstrate the dermal penetration of each of the EBDC's and ETU.

    c. Five mutagenicity studies on each of the six registered EBDC's.

    d. Mammalian cell transformation assays on each of the six EBDC's and ETU.

With the issuance of the Decision Document, the Agency concluded the Special Review and returned the EBDC's to the registration process on the condition that registrants comply with the label changes and data requirements specified in the Decision Document.

Since issuance of the Decision Document, the Agency has issued seven data call-in notices for metiram as follows:

1. January 17, 1983: This notice required the submission of the metabolism, dermal penetration and mutagenicity data identified in the 1982 Decision Document.

2. July 25, 1984: This notice advised registrants of the Agency's concern about the existence of pesticides in ground water and the designation of a number of chemicals, including metiram, which may have the potential to contaminate ground water. The chemicals were designated based on such factors as chemical structure, solubility, and use patterns. The notice required submission of certain environmental fate and product chemistry data for the agricultural uses only.

3. October 19, 1984: This notice required dietary exposure, product chemistry and toxicological (subchronic feeding and inhalation) data considered necessary to reassess the registration status of metiram.

4. March 20, 1985: This notice required registrants of all pesticide products containing metiram to submit all outstanding data requirements as outlined under 40 CFR 158 regulations for disciplines including product chemistry, toxicology, wildlife and aquatic organisms, and environmental fate.

5. April 30, 1985: This notice required additional data, not identified in the October 1984 call-in notice, but considered necessary to the reassessment of the chemicals. These data were additional toxicological (subchronic feeding and inhalation - ETU) and residue data for ETU as well as metiram.

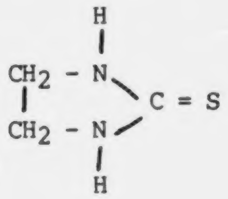
6. March 31, 1987: Residue chemistry data were required in the October 19, 1984 Data Call In Notice. Because adequate storage stability data were not submitted to ascertain whether residues of metiram and/or ETU are stable in or on plant commodities when stored, firm conclusions on dietary exposure to metiram or ETU from the use of metiram could not be drawn based on data available at that time. Therefore, this DCI required storage stability data and crop residue data for metiram and ETU.

7. April 1, 1987: This notice required additional data necessary to support the continued registration of metiram. These data requirements pertain in general to the comprehensive review of the chemical which included the reassessment of tolerances. This data included environmental fate, product chemistry, residue chemistry, toxicology and wildlife and aquatic organisms.

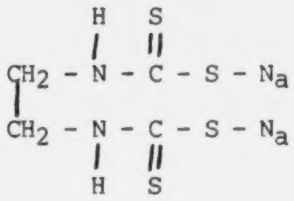
FIGURE 1

CHEMICAL STRUCTURE OF EBDC'S AND ETU

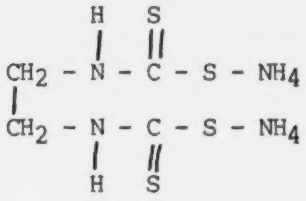
ETHYLENE THIOUREA (ETU)



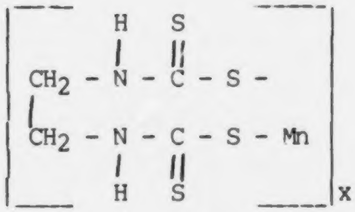
NABAM



AMOBAM



MANEB



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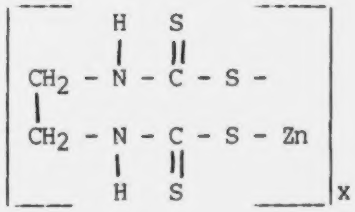
ZINEB



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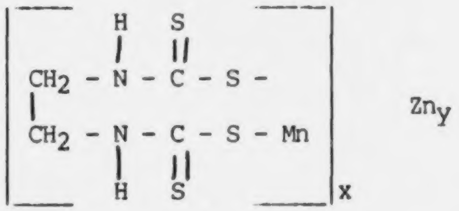
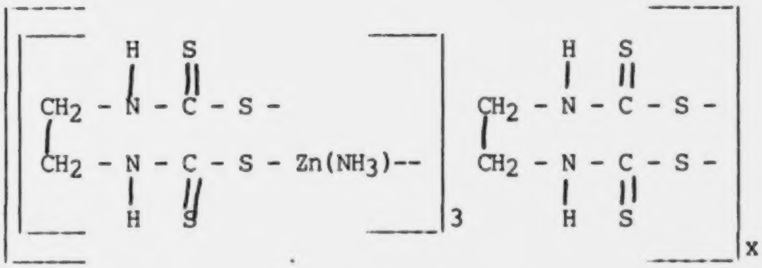
MANCOZEB



METIRAM



x > 1

The data required by the first five call-in notices to support the continued registration of metiram products have been received and considered by the Agency in its evaluation of metiram, as presented in the assessment section of this Standard. Data submitted in response to the April 1, 1987, Notice was such that the time frames for submission of data were too late for the data to be reviewed and consequently are not included in this Standard. However, all metiram data submitted are being reviewed and the registrant(s) will be informed as to the results of the Agency review when completed.

In June 1987, the Agency initiated another Special Review for the EBDC'S. The Agency initiated this Special Review of the EBDC pesticides because of concern about the oncogenic risk to consumers from dietary exposure to ETU from foods treated with these pesticides, and the risks of teratogenicity and adverse thyroid effects to applicators and mixer/loaders from exposure to ETU. ETU is present as part of the residue of the EBDC pesticides on or in treated agricultural commodities. In addition, a portion of the EBDC pesticide residues convert into ETU in the body after ingestion. At the time of initiating the Special Review, the Agency estimated that the lifetime dietary oncogenic risk to consumers from these two sources of exposure to ETU was 2.2×10^{-5}. This estimate is based on exposure to ETU from the residues of only one of the EBDC pesticides, mancozeb. Consequently, the overall dietary risk may be higher due to contributions from the other EBDC's.

III. AGENCY ASSESSMENT

A. SUMMARY

Based on the review of available data, the Agency has reached the conclusions set forth in this Standard. A summary of those conclusions follow. A more detailed discussion is contained in the remainder of this Chapter.

1. A major toxicological concern from exposure to metiram is the hazard to the human thyroid from presence of ethylenethiourea (ETU), a contaminant, degradation product, and metabolite present in metiram and other EBDC products. Additional chronic studies on metiram are required for further evaluation.

2. ETU has caused developmentally toxic/teratogenic effects in rats and hamsters. There are no adequate teratology studies on metiram. A rat teratology study on metiram may partially fill the teratology requirement if additional information on stability and homogeneity on metiram technical can be provided. No teratogenic effects associated with metiram administration were noted in this study. A rabbit teratogenicity study is required with metiram in order to fully assess its teratogenicity.

3. ETU has been classified as a Group B2 carcinogen in accordance with the Agency's Guidelines for Carcinogen Risk Assessment (September 26, 1986, 51 CFR 33992), based on studies which show that it induced an increased incidence of thyroid adenomas and adenocarcinomas in rats and hepatomas in mice.

4. In June 1987, the Agency initiated a second Special Review for the EBDC's because of concern about the oncogenic risk to consumers from dietary exposure to ETU from foods treated with these pesticides, and the risks of teratogenicity and adverse thyroid effects to applicators and mixer/loaders from exposure to ETU.

As a result of this review, the Agency has identified missing data needed to further evaluate the environmental and human risks associated with the use of metiram. These data must be submitted in order to maintain registrations of products or register new products containing metiram. Almost all of these data have been required in previous Data Call In Notices. Complete details can be obtained by referring to the tables in Appendix I.

The Agency has also determined that certain label restrictions or revisions are necessary in order for metiram products to remain in compliance with FIFRA, as indicated below. Chapter

IV, Section D, Labeling, contains the specific wording for each of the labeling statements and identifies the products to which each labeling statement applies.

- ° Protective clothing requirements
- ° Environmental hazard precautions
- ° Reentry intervals
- ° Worker safety rules
- ° Preharvest interval emphasis
- ° Grazing restrictions

The regulatory Position and Rationale section discusses the Agency's position regarding metiram.

B. PRELIMINARY RISK ASSESSMENT

Toxicology Studies - Metiram. In its review of metiram, the Agency has considered the available data as summarized below:

1. Acute Toxicity and Irritation Studies. No data were available for the evaluation of the acute toxic effects of Metiram Technical. Data are required to assess the acute oral, acute dermal, and acute inhalation toxicity, primary eye and dermal irritation and skin sensitization potential of metiram.

2. Subchronic Testing

Oral (Rodent, Nonrodent) Studies. Studies submitted in response to the Data Call In Notice of October 19, 1984, may satisfy these data requirements if additional information on the stability and homogeneity of metiram technical is provided.

In a 13-week feeding study, metiram was fed to Sprague-Dawley rats at levels of 0, 50, 100, 300, or 900 ppm (0 2.5, 5, 15, 45 mg/kg/day). Hind-limb paralysis was observed in the high dose females but not males. Atrophic lesions of thigh muscle were increased in males receiving 900 ppm and in females receiving 300 or 900 ppm (15, 45 mg/kg/day) after 13 weeks. Weight gains for these groups were also significantly decreased during the first 3 weeks of the study. Serum thyroxine levels were decreased after 11-12 weeks in males and females receiving 300 or 900 ppm (15, 45 mg/kg/day), and [^{131}I] uptake by the thyroid (measured at week 13) was decreased compared to controls in all dosed groups of males and in females receiving 100, 300, or 900 ppm (5, 15, 45 mg/kg/day). There was a minimal degree of thyroid follicular hyperplasia in 2 of the 15 males receiving 900 ppm (45 mg/kg/day). After withdrawing the test compound for a 6-week period there was a reversal of all effects noted except skeletal muscle lesions in high-dose females. The LEL, based on thyroid function tests, is 100 ppm (5 mg/kg/day) in females and 50 ppm in males; a NOEL was not achieved for males but is considered to be 50 ppm (2.5 mg/kg/day) in females.

Information on the purity and stability of the metiram test substance is needed to complete evaluation of these studies.

In a 26 week feeding study, metiram was orally administered to Rhesus monkeys at dosage levels of 5, 15, 75 mg/kg/day. There were decreased serum levels of 3,3', 5,5'-tetraiodothyronine (T_4) (a thyroid hormone) in males and females and increased thyroid weights in males at all dose levels. Decreased serum levels of 3,5,3'triiodothyronine (T_3) (a thyroid hormone) in males and females, increased thyroid weights in females, and follicular epithelial hyperplasia of the thyroid in males and females were observed in the 15 and 75 mg/kg/day groups. T_4 serum levels in 75 mg/kg/day animals appeared reversed after 5 weeks of recovery; however, this effect was not consistent at 15 weeks. Thyroid hyperplasia showed some reversibility by week 15 of the recovery period.

When metiram was orally administered to a second set of Rhesus monkeys (2/sex/dose) for 27 weeks at dosage levels of 5 and 75 mg/kg/day to assess the effect on thyroid function, there was an initial reduction in iodine uptake in males and females at 5 and 75 mg/kg/day followed by a significant increase in iodine uptake in high-dose males and females after 27 weeks of dosing.

Based on thyroid function studies and increased thyroid weights, the LEL is 5 mg/kg/day, the lowest dose tested. This study did not provide a basis to establish a NOEL for metiram.

The subchronic oral studies may be upgraded with stability and purity information on the test substance. Since a chronic, non-rodent study is required, further subchronic studies in non-rodents will not be necessary.

Dermal Studies - No data were available for the evaluation of the subchronic dermal effects of metiram. A 21-day dermal toxicity study is required.

Subchronic Inhalation - Sufficient data are available to satisfy this data requirement for metiram technical. Metiram was administered to rats in a 13-week inhalation study at levels of 0, 2.1, 20 and 101 mg/m^3 to groups of 28 males and 28 females. Group mean body weights in high dose males were significantly lower than controls from weeks 7 through 12 and in high-dose females during weeks 12 and 13. A slight decrease in body weight was observed in mid-dose males (20 mg/m^3) and females. Thyroxine and TSH were found to be slightly decreased in high-dose males and females. Blood urea nitrogen levels were significantly increased in high-dose females compared to controls, but were apparently within the range (of age and strain) of historical controls. Results of urinalysis and pathology at sacrifice showed metiram is excreted in the urine and high quantities were found in lung tissue, increasing with dosage. Several significant organ weight effects were noted including increased relative brain/bodyweight ratio, increased lung/trachea ratio in males and lowered liver weight, and lower relative liver/bodyweight ratio in high-dose males compared to controls. In females, in the high-dose group, lung/trachea weight was significantly greater than controls. In the 13-14 animals sacrificed at 13 weeks a significant number showed pigmentation of the kidneys in the convoluted tubule epithelium [11/11 males examined at the high dose vs. 0/11 controls (none were examined at the mid-dose)]. Lung alveolitis was found in 10/10 mid-dose and 10/11 high-dose males compared to 0/11 controls. Females showed an incidence of kidney pigmentation similar to males, with 10/10 high-dose and 8/10 mid-dose females compared to 0/10 controls. The NOEL (based on alveolitis found in mid- and high-dose male and female rats) was 2.1 mg/m^3 and the LEL effect level was 20 mg/m^3.

No further subchronic inhalation studies are required at this time.

3. Chronic Testing

Chronic Toxicity Studies. Metiram was fed to CD rats at dietary levels of 0, 5, 20, 80, or 320 ppm (0, .25, 1, 4, 16 mg/kg/day) for two years. The only compound-related effect observed was an increase in skeletal muscle atrophy in males and females receiving 320 ppm. There were no effects of dosing on survival, body weights, or clinical laboratory findings. Fluctuations of triiodothyronine (T3) or thyroxine (T4) serum levels, and thyroid function (as assessed by $[^{131}I]$ uptake) were observed. However, the data on T3 and T4 serum levels cannot be adequately evaluated since they were not measured on the same animals throughout the study. Based on skeletal muscle atrophy, the LEL is considered to be 320 ppm (16 mg/kg/day) and the NOEL is 80 ppm (4 mg/kg/day) metiram in the diet. This rat study may be upgraded if additional information on stability and homogeneity of metiram technical is provided.

No data are available on the chronic toxicity of metiram to non-rodents. Chronic studies in both rats and dogs are required.

Oncogenicity Studies-Rats. Data on the oncogenicity phase of the 2-year rat feeding study (also described under chronic toxicity) indicated that under the testing conditions, metiram was not oncogenic in CD rats. However, it appears that the maximum tolerated dose was not approached in this study. At the highest dose tested (320 ppm) (16 mg/kg/day) the only effect noted was an increased incidence of minimal to moderate muscle atrophy of the thighs in males and females. Dose levels were selected on the basis of the 13 week subchronic feeding study in rats which used doses up to 900 ppm (45 mg/kg/day). Decreases in serum thyroxine levels in males and females and decreased [^{131}I] uptake by the thyroid at all doses were several observations noted in the 13 week study. Based on these and other observations the Agency believes the choice of 320 ppm (16 mg/kg/day) as the highest dose is low.

Zymbal gland squamous cell carcinoma was observed in several treated males (2 in each of the low, medium-low, and medium-high dose groups; one in the high dose group) and in one female of the mid-dose group but none in the control groups. However, because of the lack of historical background incidence of this tumor in this strain of rat, the significance of this incidence could not be evaluated. Analyses of test substance for stability, homogeneity and purity were not reported.

Mice

In a 1979 oncogenicity study, CFLP mice were fed 0, 100, 300, or 1000 ppm (0, 15, 45, 150 mg/kg/day) of the test material in the diet. A compound-related oncogenic response was not apparent. However, this study could not be fully evaluated because of the following deficiencies:

a. The summary tabulation of histopathology data did not list the number of tissues examined, only the number of animals.

b. Examination of a sampling of individual pathology data records indicated that many essential tissues may not have been examined histologically.

c. Historical laboratory data for neoplasms in the CFLP strains of mouse were not provided.

The data as presented are inconclusive. In addition, the maximum tolerated dose was apparently not reached in this study since the highest dose level failed to induce any overt toxic effects in both sexes; the animals could have tolerated higher dose levels. Analyses of the test substance for stability and homogeneity were not reported. If adequate histopathology information and stability information on the test substance cannot be provided, a repeat study will be necessary.

These studies may suffice if additional information on the selection of dose (for mouse and rat studies), on histopathology (for the mouse study), and on stability, homogeneity and purity on Metiram Technical (for both mouse and rat studies) can be provided.

Teratogenicity Testing In a 1979 teratogenicity study in Sprague-Dawley rats, metiram was administered at 0, 40, 80, and 160 mg/kg/day to 20 female rats per group. Maternal body weight gains for high dose dams were significantly reduced on gestation days 10 and 14 when compared with controls. No teratogenic effects associated with metiram administration were noted in this study.

Maternal toxicity no observed effects level (NOEL) was 80 mg/kg/day with bodyweight changes in high-dose dams 15 and 16% lower than controls on treatment days 10 and 14. Based on the above findings, the LEL for maternal toxicity was 160 mg/kg/day. The lowest observed effect level for developmental toxicity was assessed at 160 mg/kg/day and the NOEL was 80 mg/kg/day based on preimplantation and postimplantation losses. At the high dose these values were 13.3% and 6.9%, respectively, with corresponding control values of 5.9% and 4.0%. No teratogenic effects associated with metiram administration were noted in this study. This study was inadequate for complete evaluation, but may be acceptable if adequate stability and homogeneity on metiram technical are provided.

A rat and rabbit teratology study are required. The rat study failed to include information on stability and homogeneity on metiram technical; if this is provided, the study may not have to be repeated.

Reproduction Study In a reproduction study with Sprague-Dawley rats, metiram mixed in the diet at concentrations of 0, 5, 40, and 320 ppm (0, .25, 2, 16 mg/kg/day) produced mild decreases in parental bodyweights and parental food consumption at 320 ppm. In addition, the following effects in reproductive performance and developmental effects were noted: 1) Litter size for animals dosed with 5, 40, and 320 ppm were reduced compared with controls for the F_{2b} and F_{3b} (significant at all dose levels); however these reductions did not occur in dose-related patterns. 2) The mating performance of animals dosed at 320 ppm (16 mg/kg/day) was slightly reduced when compared with controls; the length of gestation at this dose level was slightly increased when compared with controls. 3) Based on the above findings, the NOEL for parental toxicity of metiram is assessed at 40 ppm, (2 mg/kg/day) and the LEL is 320 ppm (16 mg/kg/day). A NOEL for developmental toxicity was not established in this study; effects were seen at all dosage levels (reduced litter size). Also mating performance was reduced at the high dose in the F_3 generation. Because of the lack of a NOEL for reproductive effects, the submitted study does not satisfy the data requirements. A new study is required.

Mutagenicity Studies - Metiram was tested for its potential to induce unscheduled DNA synthesis in the primary hepatocyte in rats. Under the test conditions, "the test material did not induce significant changes in the nuclear labeling of rat primary hepatocytes in concentrations ranging from 0.492 to 49.2 ug/ml of the test material and 25.8% to 107.2% cell survival rate."

In an in vivo bone marrow cytogenetic assay in rats, the acute (one dose) or subacute (daily x 5 days) oral exposure to male rats to 2.4 or 0.2 g/kg, respectively, of metiram technical did not cause a significant increase in chromosomal aberrations from bone marrow cells sampled over the entire mitotic cycle.

The following studies were submitted in response to an earlier Data Call In Notice with the results given and the Agency's classification of the study:

a) S. Cerevisiae reverse mutation (presumptive positive) (inconclusive/unacceptable)
b) UDS/rat primary hepatocytes (negative) (acceptable)
c) In vivo bone marrow cytogenetic assay/rat (negative) (acceptable)
d) Transformation/promotion in C3H 10 T 1/2 cells (negative/weak positive) (acceptable/inconclusive)
e) Mouse/host-mediated assay (negative) (acceptable)
f) In vitro SCE in CHO cells (positive without S9, and with mouse S9; negative with rat S9) (acceptable)
g) Point (gene) mutation (HGPRT) in CHO cells (positive without S9, marginal positive with rat S9) (inconclusive) A repeat assay (point mutation in CHO cells) is required.

The majority of acceptable mutagenicity studies on metiram were negative. However, the in vitro sister chromatid exchange assay in CHO cells was positive and is considered a sensitive test for chromosomal effects. Metiram is considered positive for chromosomal damage.

Metabolism Studies - The metabolism and clearance of metiram were studied in male and female CD rats. The data indicate that the polymer is hydrolyzed and readily absorbed and eliminated in the urine and feces. Elimination in the urine is slightly higher in females than in males. Residues were highest in the thyroids, kidneys, and gastrointestinal (G.I.) tract and were higher in the tissues of female rats than male rats. Some accumulation of residues in the tissues was seen after repeated dosing of [^{14}C] Metiram (seven daily oral dosages at 5 mg/kg/day). Analysis of metabolites indicates that metiram is catabolized to numerous compounds of low molecular weight.

ETU was reported to be one of the metabolites in the urine and bile of rats dosed with radiolabeled metiram mixtures. ETU was reported to comprise roughly 30 percent of the 0-24 hour urinary radioactivity and 4.2 to 18.0 percent of the 0-12 hour biliary radioactivity.

Percutaneous Absorption - Metiram technical is not significantly absorbed through the skin. [^{14}C] Metiram was not significantly absorbed when topically applied to the shaved skin of adult male CD-1 rats. Less than 1 percent of the 240 mg/kg dose of [^{14}C] metiram was absorbed through the skin after 8 hours of contact. In contrast, at a dose level of 0.24 mg/kg a higher percentage of the radioactivity was absorbed (about 5 fold). A dermal absorption factor of 6 percent was employed in the risk assessment based on the exposure to applicators.

Toxicological Studies - ETU - Since ETU, a contaminant, degradation product, and metabolite of metiram and other EBDC products, presents toxicological concerns, available data on ETU were considered in the overall evaluation of metiram. These data are summarized as follows:

Subchronic Studies - During a 90-day rat feeding study with mancozeb, an additional group of animals received 250 ppm (12.5 mg/kg/day) ETU. Compound related effects in this group were generally comparable to those observed at 1000 ppm (50 mg/kg/day) mancozeb (depressed body weight and changes in hormone levels accompanied by diffused hyperplasia of thyroid follicular epithelium). Residue analysis for ETU in mancozeb-treated animals revealed that no ETU was present in the blood.

In a rat study conducted to examine the subchronic effects of ETU on the thyroid, levels of 50, 100, 500, and 750 ppm (2.5, 5, 25, 37.5 mg/kg/day) ETU were fed for 30, 60, 90, and 120 days. A NOEL was not determined in this study due to effects of ETU seen on thyroid weights at all dosage levels at 120 days. In a second rat study, levels of 0, 1, 5, 25, 125, and 625 ppm (.05, .25, 1.25, 6.25, 31.25 mg/kg/day) ETU were fed for 30, 60, and 90 days. Thyroid hyperplasia, decreased uptake of ^{125}I by the thyroid, and decreased serum T_3 (triiodothyronine) and T_4 (tetraiodothyronine) were seen. The LEL was 25 ppm (1.25 mg/kg/day) for these effects with 5 ppm (0.25 mg/kg) considered the NOEL.

In a 90-day mouse study, ETU fed at levels of 0, 1, 10, 100, and 1000 ppm (0, .15, 1.5, 15, 150 mg/kg/day) resulted in increased thyroid weights in females and an increased incidence of follicular cell hyperplasia in both sexes at levels of 100 ppm (15 mg/kg/day) and higher. Liver toxicity was only observed at the highest level, 1000 ppm (150 mg/kg/day).

In a 21-week study in Rhesus monkeys, at dosage levels of 0, 2, 10, 50, and 250 ppm (0, 0.1, 0.5, 2.5, 12.5 mg/kg/day), serum thyroid hormone concentrations were measured as well as iodine uptake in the thyroid. Mild to moderate pituitary hypertrophy was seen at 50 and 250 ppm, as well as thyroid follicular lining cell hypertrophy and hyperplasia (mild at 50 ppm; moderate to severe at 250 ppm). Serum levels of T_4 were significantly decreased in the 250 ppm group. Free serum T_4 levels were also significantly decreased in both the 50 and 250 ppm group; iodine uptake was significantly increased at these levels and thyroid stimulating hormone (TSH) levels were significantly increased at 250 ppm.

In a 6-month Rhesus monkey study, at dosage levels of 0, 50, 150, and 450 ppm (0, 2.5, 7.5, 22.5 mg/kg/day), pituitary as well as thyroid hormone levels were measured. A NOEL was not demonstrated.

Oncogenicity Studies - Three oncogenicity studies have been reviewed, as discussed below:

In a mouse study (Innes), two hybrid strains of mice were used [(C57BL/6 x C3H/Anf)F_1 (Strain X) and (C57BL/6 x AKR)F_1 (Strain Y)]. Eighteen mice per sex per group were used in the treatment group. Only one dose was tested which was stated to be the maximum tolerated dose. When the mice were 7 days old, 215 mg/kg ETU was given by stomach daily. At 28 days of age, the mice were given diets containing 646 ppm (96.9 mg/kg/day) of ETU. The mice were sacrificed after a total of 83 weeks of treatment. Histopathology consisted of examination of all major organs and of all grossly visible lesions. Thyroid glands were not examined. The incidence of liver tumors, which were not classified as adenomas or carcinomas but only as hepatomas, is outlined in the following table:

	Male		Female	
	Control	Treated	Control	Treated
Strain X	3/14	14/16	0/18	18/18
Strain Y	1/18	18/18	0/18	9/16

Totals: Controls - 4/68 Treated - 59/68

In a study with Charles River CD-1 rats, 175 or 350 ppm (8.75, 17.5 mg/kg/day) ETU was administered in the diet for 18 months. At that time, 5 rats/sex were sacrificed and the remaining rats were placed on control diets until termination of the study at 24 months. The control group consisted of 32 male and 36 female rats. No thyroid lesions were seen in the control group. The incidence of thyroid lesions in the ETU-treated rats is presented below. The number of animals examined was not given.

	350 ppm		175 ppm	
Lesion	Males*	Females	Males*	Females
Thyroid carcinoma** (follicular)	17	8	3	3
Thyroid solid cell ademona	0	1	0	2
Hyperplastic goiter	17	13	9	6
Simple goiter	2	4	4	2

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*All five male rats in the high-dose group sacrificed at 18 months had hyperplastic goiter; 3 had follicular thyroid cancer.

**Two with lung metastases.

In a 2-year study, Charles River rats were placed on diets containing 0, 5, 25, 125, 250, or 500 ppm (0, .05, .25, 6.25 12.5, 25 mg/kg/day) ETU. Body weight gain was adversely affected at the highest dose tested at 18 and 24 months for both males and females. ^{131}I uptake was statistically increased in male rats at 18 months in the 25 and 125 ppm (.25, 6.25 mg/kg/day) groups and decreased at 500 ppm (25 mg/kg/day). At 24 months in the male rats, ^{131}I uptake was significantly increased in the 5 ppm (.05 mg/kg/day) group and decreased in the 500 ppm (25 mg/kg/day) group. Because of large variability in the values obtained, there were no statistically significant differences in ^{131}I uptake in female rats.

Histopathology incidence data were combined for males and females. An increase in the number of rats with cataracts/ keratitis and with thyroid follicular adenocarcinoma/ carcinoma was observed in the groups fed 250 and 500 ppm (12.5, 25 mg/kg/day) ETU; with thyroid adenomas in the 250 ppm (12.5 mg/kg/day) group; and with thyroid hyperplasia in the 5, 25, 125, and 250 ppm (.05, .25, 6.25 mg/kg/day) groups. The LEL is 5 ppm (0.25 mg/kg/day) for the effects of ETU on the thyroid in this study. Relevant data are summarized as follows:

Tumor Incidence Data for Rats, Including 18-Month Interim Sacrifice, Fed ETU in the Diet

	Dose Levels in ppm					
	0	5	25	125	250	500
Pathological lesions						
Cataracts/keratitis	2	1	0	2	6	12
Thyroid carcinoma/ adenocarcinoma (follicular)	2	2	1	2	16	62
Thyroid adenomas	2	--	5	1	21	3
Thyroid hyperplasia	4	20	41	44	27	3
Parathyroid hyperplasia	6	11	8	2	3	0
Number of Rats per Group	72	75	73	73	69	70

Statistics were not reported on the histopathological data. Historical control data were not available. More detailed information on this study is not available.

Teratology Studies - ETU has been shown to be a teratogen in studies with rats and hamsters. In rats, it produces a wide variety of anomalies in the central nervous, urogenital and skeletal systems as well as other organs at dosages that do not produce maternal toxicity or fetotoxicity. The NOEL for these effects is 5 mg/kg. Administration of T_3/T_4 with ETU to pregnant rats appears to reduce the incidence of some of these effects.

Mutagenicity Studies - Results of short-term assays indicate that ETU is weakly genotoxic; ETU has been shown to give mixed results for gene mutation in both bacterial and mammalian cell lines, but positive results for DNA repair in human cells, yeast, and bacteria. Although reportedly positive in one mammalian cell transformation assay using hamster cells, an adequate assay in mouse cells was negative.

Metabolism Studies - In a study with Rhesus monkeys, 50 percent of an administered dose of ^{14}C-ETU was excreted in the urine within 24 hours and 90 percent within 72 hours. Only 0 to 0.68 percent of the label was eliminated in the feces at 24 hours and no radioactivity was found at the 48- and 72-hour sampling periods.

In another study with Wistar rats, ^{14}C-ETU was predominantly excreted in the urine. The ratio of urine to fecal excretion varies with dose, (i.e., for 0.1 ppm ETU the ratio was 55/25, and at 10 ppm ETU the ratio was 70/10). Minimal radioactivity was recovered as $^{14}CO_2$ ($\leq$ 0.5%). The level of radioactivity plateaued in the thyroid gland after 8 days of dosing and declined rapidly once dosing was terminated.

Structure Activity Information - ETU is structurally related to thiourea, methimazole, propylthiouracil, and thiouracil, and thyroid inhibitors. Chronic studies on thiourea in rats have shown that it induces hepatomas and thyroid enlargement. Methimazole, propylthiouracil and thiouracil all induce thyroid tumors in rats. Propylthiouracil also induces thyroid tumors in hamsters and guinea pigs and pituitary adenomas in mice. Thiouracil induces hepatomas and thyroid tumors in mice.

Risk Assessment - The Agency does not have any acceptable oncogenicity data on metiram. However, based on the data available on ETU, as discussed in the preceding section, the Agency has classified ETU, in accordance with the Agency's Guidelines for Carcinogen Risk Assessment (September 26, 1986, 51 FR 33992), as a Group B2 oncogen, Probable Human Carcinogen.

The Agency's classification of ETU was made in accordance with its guidelines for carcinogen risk assessment. These guidelines categorize the evidence on carcinogenicity of chemicals in terms of how likely it is that the chemical is a human carcinogen. Under this scheme, Group B2 categorization is appropriate if there is "sufficient evidence" of the chemical's carcinogenicity from animal studies. "Sufficient evidence" is defined as an increased incidence of malignant tumors (or combined malignant and benign tumors) in multiple species or strains, in multiple experiments, or to an unusual degree with regard to incidence, site or type of tumor, or age at onset.

ETU induced an increased incidence of thyroid adenomas and adenocarcinomas in two separate studies with rats and hepatomas in two strains of mice. Furthermore, ETU induced the thyroid tumors in rats after 1 year or less of treatment and induced both the thyroid tumors in rats and the hepatomas in mice to an unusual degree in a single experiment.

The classification as a Group B2 oncogen is also supported by positive structure-activity data since several other thyroid inhibitors (i.e., thiouracil and thiourea) have been found to induce hepatomas and/or thyroid tumors in rodents.

EPA acknowledges that the studies considered in arriving at its classification of ETU were not carried out in accordance with EPA guidelines for oncogenicity studies. EPA, however, does consider the studies adequate to conclude that ETU is oncogenic to rats and mice due to the magnitude of the response seen. The Agency's conclusions regarding the classification of ETU will be reconsidered when results of additional studies on ETU are available.

Worker Exposure and Risks - The Agency is currently assessing risks associated with systemic effects of metiram and the teratogenic, thyroid and oncogenic effects attributable to ETU. Information available to the Agency about use practices indicates that aerial loading and application are generally performed by different people. For other application methods (ground boom, airblast, sprinkler and seed treatment), loading and application are generally performed by the same person. Mixer/loaders and applicators are also exposed to ETU when the EBDC pesticides are used in a tank mix. Available data indicate that the concentration of ETU as a contaminant can vary between products. For calculating direct exposure to mixers and loaders while preparing and loading metiram spray mixture, the Agency used 0.1% of the metiram exposure. This represents the typical level of ETU contamination of EBDC products for which we have data. The pesticide applicator is exposed not only to the amount of ETU which contaminates the technical and tank mix but also to the additional ETU formed while spraying. There are no available data for metiram, therefore, the Agency used the available data for maneb to calculate direct ETU exposure to applicators.

Metiram

An oral subchronic study of metiram in rats showed thyroid effects at the lowest dose tested (2.5 mg/kg) in male rats. No teratogenic effects were seen at the highest dose tested

(160 mg/kg/day) when metiram was tested in the rat. The Agency calculated a ratio for metiram exposure to the lowest dose level for the subchronic thyroid effects; however, this is not a true MOS as no NOEL was found for males in the rat study. Only for oncogenicity, for which the Agency has no studies for metiram, was a metabolic conversion to ETU performed. The Agency also calculated MOSs for teratogenic and thyroid effects of ETU from direct exposure to ETU as an impurity and environmental degradate from the use of metiram. In these calculations, dermal absorption figures of 30% and 6% were used for ETU and metiram, respectively. See Table 2.

ETU - ETU has been shown to be teratogen in studies with rats and hamsters. In rats, it produces a wide variety of anomalies in the central nervous, urogenital and skeletal systems. The NOEL for these effects is 5 mg/kg.

In assessing teratogenic margins of safety, the Agency has assumed 30 percent dermal absorption based on a dermal absorption study for the ETU contaminant in the tank mix. Because metiram did not demonstrate teratogenic effects at 160 mg/kg/day, we did not perform an in vivo conversion calculation. The exposures to applicators and the margins of safety for teratogenic effects of ETU from exposure to metiram and ETU in the tank mix are shown in Table 3.

ETU has also demonstrated thyroid hyperplasia, decreased uptake of ^{125}I (iodine) by the thyroid and decreased serum T_3 and T_4 in a subchronic feeding study in rats. The NOEL for these effects is 5 ppm (0.25 mg/kg/day). Margins of safety for thyroid effects were calculated for direct exposure to ETU and are given in Table 3.

The Agency has also calculated the oncogenic risk to loaders and applicators from exposure to ETU both from metiram absorbed and metabolized to ETU and from direct exposure to ETU as a contaminant in the tank mix. The exposures and risks are given in Table 3. The range of oncogenic risk is 4×10^{-8} to 3×10^{-5}.

Dietary Exposure and Risk - The Agency has assessed dietary risks attributed to exposure to ETU resulting from application of metiram to crops. Risks were calculated for certain chronic adverse effects from chronic dietary exposure to ETU and metiram. In addition, oncogenicity and teratology dietary risks were calculated for ETU.

Chronic Adverse Effects

Dietary exposure to ETU from use of metiram and potential risks for adverse effects from this exposure were assessed. Average field trial residues of ETU, obtained from studies submitted in support of metiram tolerances, were used for this dietary exposure analysis. The ETU residues for processed products were calculated by using the appropriate conversion factors, calculated from the available data, for each of the processed commodities since some metiram converts to ETU during the processing of the raw agricultural commodities. These residues were then reduced by the percent of crop treated with metiram obtained from actual usage data except a percent crop treated value of 10 was used for all commodities where the estimated percent crop treated was less than 10. The results of this analysis indicate that the average consumer in the U.S. population receives a direct dietary exposure to ETU from metiram use of 0.00008 mg/kg/day.

The PADI for ETU was derived from the 2-year chronic feeding study in Charles River rats with an LEL of 0.25 mg/kg/day. An uncertainty factor of 3,000 was applied. This resulted in a PADI of 0.00008 mg/kg/day. The effect on which the PADI is based was hyperplasia of the thyroid; a NOEL for this effect was not established for this study.

The dietary exposure to ETU of 0.00008 mg/kg/day occupies 98 per cent of the PADI.

Secondly, dietary exposure to metiram and potential risks for adverse effects were assessed. The residues used in the analysis were the average field trial residues of metiram, obtained from data submitted in support of established tolerances, considering the percent of crop treated. Based on these average residues, the average consumption estimate for the U.S. population is calculated as 0.0004 mg/kg/day metiram.

The PADI for metiram was derived from a three generation rat reproduction study with a LEL (NOEL has not been established) of 0.25 mg/kg/day and a safety factor of 1000 for a PADI of 0.0003 mg/kg/day.

The dietary exposure to metiram of 0.0004 mg/kg/day utilizes 128 percent of the PADI.

Oncogenicity Risks

A risk assessment was conducted to determine potential oncogenic risks from dietary exposure to ETU from use of metiram. For this assessment, average residues for both ETU and metiram from field trials were used. The Agency's Carcinogen Assessment Group derived risk models based on various bioassays on ETU. The most sensitive sex/species end point was found to be male mouse liver tumors in the Innes study. The potency, or Q_1^*, was calculated to be 0.14 $(mg/kg/day)^{-1}$.

Using the Tolerance Assessment System (TAS), the dietary exposure analysis indicates that the average consumer in the

TABLE 2
NONDIETARY RISK ASSESSMENT FOR METIRAM

		mg/kg/day METIRAM DERMAL EXPOSURE	mg/kg/day a/ METIRAM ABSORBED DERMALLY	mg/kg/day METIRAM INHALATION EXPOSURE	METIRAM TOTAL DAILY EXPOSURE mg/kg/day	mg/kg/day b/ METIRAM METABOLIZED TO ETU	mg/kg/day ETU DERMAL EXPOSURE	mg/kg/day c/ ETU ABSORBED DERMALLY	mg/kg/day ETU FROM INHALATION EXPOSURE	ETU TOTAL DAILY EXPOSURE mg/kg/day
APPLES:										
AERIAL	LOADER	0.2300	0.0138	0.0035	0.0173	0.0035	0.0002	0.0001	0.0000	0.0035
	APPLICATOR	0.0081	0.0005	0.0003	0.0008	0.0002	0.0140	0.0042	0.0000	0.0044
AIRBLAST	LOADER	0.9400	0.0564	0.0140	0.0704	0.0141	0.0009	0.0003	0.0001	0.0144
	APPLICATOR	2.2000	0.1320	0.0033	0.1353	0.0271	0.1300	0.0390	0.0000	0.0661
	COMBINE	3.1400	0.1884	0.0170	0.2054	0.0411	0.1309	0.0393	0.0001	0.0804
POTATOES:										
AERIAL	LOADER	1.9000	0.1140	0.0290	0.1430	0.0286	0.0019	0.0006	0.0009	0.0300
	APPLICATOR	0.0380	0.0023	0.0012	0.0035	0.0007	0.0023	0.0007	0.0000	0.0014
	FLAGGER	0.0210	0.0013	0.0120	0.0133	0.0027	0.0130	0.0039	0.0009	0.0074
GROUNDBOOM	LOADER	0.2200	0.0132	0.0034	0.0166	0.0033	0.0002	0.0001	0.0000	0.0034
	APPLICATOR	0.2900	0.0174	0.0053	0.0227	0.0045	0.0170	0.0051	0.0000	0.0096
	COMBINE	0.5100	0.0306	0.0087	0.0393	0.0079	0.0172	0.0052	0.0000	0.0130
HOMEOWNER										
ROSES	COMBINE	0.0053	0.0003	0.0000	0.0003	0.0001	0.0000	0.0000	0.0000	0.0001

a/ 6% DERMAL ABSORPTION FOR METIRAM
b/ 20% METABOLIC CONVERSION OF METIRAM TO ETU
c/ 30% DERMAL ABSORPTION FOR ETU

Table 3

NONDIETARY RISK ASSESSMENT FOR METIRAM

		METIRAM TOTAL DAILY EXPOSURE mg/kg/day	ETU TOTAL DAILY EXPOSURE mg/kg/day	DAYS EXPOSED	ETU TOTAL YEARLY EXPOSURE mg/kg	ETU TOTAL YEARLY DIRECT EXPOSURE mg/kg	METIRAM TOTAL YEARLY EXPOSURE mg/kg	SYSTEMIC THYROID SEASONAL METIR. MOS 2.5 mg/kg	MOS TERATO ETU 5 mg/kg	SYSTEMIC THYROID SEASONAL ETU MOS .25 mg/kg	a/ ONCO RISK ETU
APPLES:											
AERIAL	LOADER	0.0173	0.0035	1	0.0035	0.0001	0.0173	13006	1420	375000	1.93E-07
	APPLICATOR	0.0008	0.0044	1	0.0044	0.0042	0.0008	286260	1148	5357	2.39E-07
AIRBLAST	LOADER	0.0704	0.0144	7	0.1009	0.0024	0.4928	457	347	9454	5.53E-06
	APPLICATOR	0.1353	0.0661	7	0.4626	0.2731	0.9471	238	76	82	2.53E-05
	COMBINE	0.2054	0.0804	7	0.5631	0.2755	1.4378	156	62	82	3.09E-05
POTATOES:											
AERIAL	LOADER	0.1430	0.0300	4	0.1201	0.0057	0.5720	393	167	3961	6.58E-06
	APPLICATOR	0.0035	0.0014	4	0.0055	0.0028	0.0139	16164	3608	8152	3.04E-07
	FLAGGER	0.0133	0.0074	4	0.0296	0.0190	0.0530	4242	675	1184	1.62E-06
GROUNDBOOM	LOADER	0.0166	0.0034	7	0.0237	0.0004	0.1162	1936	1479	53571	1.30E-06
	APPLICATOR	0.0227	0.0096	7	0.0675	0.0357	0.1589	1416	519	630	3.70E-06
	COMBINE	0.0393	0.0130	7	0.0911	0.0361	0.2751	818	384	623	4.99E-06
HOMEOWNER											
ROSES	COMBINE	0.0003	0.0001	10	0.0007	0.0001	0.0032	70755	68306	234375	4.01E-08

a/ RISK = YEARLY EXPOSURE/365 X 430/70 X 0.14/mg/kg/day

U.S. population receives a dietary exposure of 0.00008 mg/kg body weight/day ETU from conversion of metiram on crops. This analysis was based on average field residues for ETU considering the percent crop treated with metiram. The potential dietary risk is calculated by multiplying exposure by the Q_1*:

$$\begin{aligned} \text{Dietary Risk} &= \text{Exposure} \times Q_1^* \\ &= 0.00008 \times 0.14 \\ &= 1.1 \times 10^{-5} \end{aligned}$$

In addition, there is dietary exposure from conversion of metiram to ETU in vivo after eating food containing metiram residues. Metabolism studies in rats show that approximately 20 percent of metiram is metabolically converted to ETU. In order to determine the dietary exposure to ETU from conversion of metiram residues in this way, the metiram dietary exposure of 0.0004 mg/kg/day is multiplied by 20 percent to yield an exposure of 7.7×10^{-5} mg/kg/day ETU. Multiplying this by the Q_1* of 0.14 $(\text{mg/kg/day})^{-1}$ yields a risk of 1.1×10^{-5}.

The total potential dietary risk from exposure to ETU from use of metiram on food crops is obtained by adding 1.1×10^{-5} and 1.1×10^{-5}.

$$\text{Total Dietary Oncogenic Risk} = 2.2 \times 10^{-5}$$

Teratogenicity Risks

Because ETU has been shown to be a teratogen in studies with rats and hamsters, an exposure and risk assessment was conducted for this effect. In rats, ETU produces a wide variety of anomalies in the central nervous, urogenital, and skeletal systems as well as other organs at dosages that do not produce maternal or fetotoxicity. The NOEL for these effects is 5 mg/kg/day.

Metiram and ETU crop residues were derived from studies submitted by the registrant. The analysis was conducted assuming that ETU was present uniformly in the food commodities at the maximum residue observed in field tests conducted closest to the maximum application rate, the minimum PHI, and the typical number of applications. The percent of crop treated was not considered because this is a single exposure rather than a lifetime exposure.

The acute dietary exposure for ETU is compared to a NOEL for teratological effects of 5 mg/kg. The population subgroup of interest is females of child-bearing age. The Margin of Safety (MOS) for acute exposure is calculated as the ratio of the NOEL to the estimated exposure. The estimate of the average MOS for females of child-bearing age is:

$$MOS = (5mg/kg) / (0.001141\ mg/kg) = 4300$$

Based on the TAS, only two percent of the females are estimated to be exposed to ETU levels exceeding 0.007 mg/kg, corresponding to an MOS of less than 700. The exposure distribution indicates that no member of the subgroup is expected to have an MOS of less than 300.

C. OTHER SCIENCE FINDINGS

Environmental Fate. Available data are insufficient to fully assess the environmental fate of metiram. Presently, only the hydrolysis, and photodegradation in soil and in water data requirements on both metiram and ETU are fully satisfied. The ETU studies were submitted in response to the Mancozeb Registration Standard and reviewed for metiram. Some aerobic and anaerobic soil metabolism, leaching and field dissipation data are also available on metiram but the data requirements for registration remain unsatisfied since additional dissipation and leaching data on ETU are required.

Metiram has a very limited solubility in water. Metiram, in water solution, degrades primarily to ETU (85%) and other transient degradates. ETU is also a soil degradate of metiram and its formation in soil is enhanced by sunlight. ETU is stable in water at pH 5-9 and under sunlight and the degradation of ETU on soil is not enhanced by sunlight radiation. ETU is the degradate of major environmental concern.

Hydrolysis - An acceptable study demonstrated that the hydrolysis of metiram results in formation of ETU as a major degradate (over 85% after 40 days at pH 5, 7, and 9). ETU is quite stable to hydrolysis at pH 5 and 7 and undergoes a slow decomposition at pH 9 to polar degradates. Ethyleneurea (EU), hydantoin and uncharacterized polar degradates are also present in small quantities. An acceptable ETU hydrolysis study indicated that no detectable degradation of ETU occurred at pH 5, 7, and 9 in 30 days. Therefore, no breakdown of ETU due to hydrolysis is expected in the environment.

Photodegradation in Soil & Water - An acceptable water photodegradation study showed that breakdown of metiram in water occurred primarily by hydrolysis and not by photodegradation. ETU was formed as a major degradate at 71% after 5 days at a somewhat faster rate than observed in hydrolysis studies. Ethyleneurea (EU) and uncharacterized polar degradates were also present in small quantities. Photodegradation does not appear to be a significant mode of degradation in water for metiram or ETU. In a separate ETU study, no significant degradation of ETU occurred at pH 7 water solution during the 30 days study period and thus no breakdown of ETU due to photodegradation is expected in the environment in absence the of photosensitizers.

An acceptable metiram photodegradation study on soil showed that product formation under exposure to xenon lamp radiation was generally controlled by soil metabolism and not by photodegradation. ETU was slightly more significant in irradiated samples and the level of ETU was maintained fairly consistent at 3.3% during the exposure period. ETU appeared quite stable under xenon lamp irradiation. Hydantoin, carbamid and EU (ethylene urea) that were also formed via soil metabolism, underwent degradation under sunlight with half-lives of less than a month. An acceptable ETU study demonstrated that the degradation pattern and rates of ETU on soil were almost identical on both exposed and non-exposed ETU fortified soil samples. Therefore, photodegradation is not expected to affect the environmental fate of ETU.

Ground water - Leaching and field dissipation data are insufficient to allow a final ground water assessment to be conducted. A 30-day aged soil leaching study was conducted, but it was not determined how much ETU was present in the aged soil prior to the application of water and whether ETU was present in the leachate. The soil column was analyzed and most of the aged residues were present in the top 10 cm of the soil column. Field dissipation studies on two sites were conducted to a depth of only 12 inches with an analytical method of limited sensitivity to 10 ppb level.

Although available aerobic and anaerobic soil metabolism data and two field dissipation studies appear to indicate that ETU degrades rapidly in soil, it has been reported that ETU has been detected in ground water in Collier County, Florida.

Because ETU is a suspected leacher and an oncogen, the Agency is requiring a small-scale retrospective monitoring study to analyze specifically for metiram and ETU.

Ecological Effects. Available data are insufficient to completely evaluate the ecological effects of metiram. The following conclusions can be made based on available data:

1. Toxicity to Birds. Based on a mallard duck and a bobwhite quail study, there is sufficient information available to characterize metiram on an subacute dietary basis as slightly toxic to birds. Formulated metiram showed that LC50 values for mallard duck and bobwhite quail are both greater than 3712 ppm.

2. Toxicity to Fish, Aquatic Invertebrates, and Estuarine/Marine Organisms. No data were available in this area at the time of this review. Studies have recently been submitted and are under review.

3. Effects on Beneficial Insects. Based on an acute contact honeybee toxicity study, there is sufficient information to characterize metiram as practically nontoxic to honeybees.

Metiram has been characterized as slightly toxic to two species of birds tested and practically nontoxic to honeybees. It is generally unstable in the moist environment and biological systems, and degrades rather rapidly to ETU in water. The maximum Estimated Environmental Concentrations (EEC's) from runoff of metiram in one acre pond (6-foot deep) are 9.8 ppb and 42.9 ppb for potato end-use and apple end-use, respectively. However, there are no other fish and wildlife toxicity data and chemical fate information available. Therefore, a risk assessment of metiram for these kinds of effects, is deferred due to lack of complete fish and wildlife toxicity data and environmental fate information.

Reentry Consideration. Toxicity and exposure criteria are set forth in 40 CFR 158. If a chemical meets the specified criteria, reentry data are required.

Metiram does not meet the acute toxicity criteria, and there is no epidemiological evidence that residues of this pesticide cause adverse effects on persons entering treated sites. However, ETU has demonstrated evidence of oncogenicity, mutagenicity, teratogenicity and thyroid effects. Therefore, the chronic toxicity criteria have been met. Metiram also meets the exposure criteria in that it is registered for use on crops which may involve substantial exposure to residues of the pesticide. Reentry data are required. An interim 24-hour reentry interval requirement is imposed until the required data are submitted and evaluated and a change in this reentry interval is announced.

D. TOLERANCE REASSESSMENT

Tolerances, expressed as zinc ethylene bisdithiocarbamate equivalents, have been established for residues of metiram in a variety of raw agricultural commodities and meat byproducts (40 CFR 180.217 and 180.319). EPA has evaluated the residue and toxicology data supporting these tolerances. The following were considered during this evaluation:

- Whether the current tolerances and food additive regulations are sufficient to cover the actual residues resulting from use (including FIFRA section 24(c) and intrastate uses).
- Whether group tolerances can be established in accordance with 40 CFR 180.34(f).
- Whether, in the absence of tolerances, restrictions on use, grazing, or feeding of treated commodities are necessary.
- Whether the tolerances are expressed accurately and in current terminology.

The regulatory results of the Agency's review are set out in Section IV.A., Regulatory Positions and Rationales.

Residue Data. The residue data reviewed in support of these tolerances include the following:

1. Data on the nature of the residues in both plants and livestock, including identification of major metabolites and degradates of metiram. The metabolism is not completely understood. Metabolites identified thus far include ethylenethiourea (ETU), ethyleneurea (EU) and hydantoin (HT), ethylenediamine (EDA), 3-(2-imidazolin-2-yl)-2-imidazolidinethione, glycine and oxalic acid. Additional data are required.

2. Analytical methodology for determining the levels of residues of metiram in plants and animals. Present colorimetric CS_2 evolution methods are adequate for collection of data pertaining to residues of metiram in or on plant and animal commodities. However, none of the colorimetric methods are specific for metiram and are therefore inadequate for enforcement purposes. Additional data are required.

3. Storage stability data. Some storage stability data was submitted in response to the March 31, 1987 Data Call In Notice. These data have been screened and are being reviewed. The Agency concludes that it is prudent to require storage stability data be conducted concurrently with residue

analysis for each laboratory conducting residue studies, and for each crop for which studies are required in this Standard. Additional storage stability data are required.

4. Data on the magnitude and levels of residues of metiram in individual raw agricultural commodities, animal products and processed food and feed items. Data are inadequate to support tolerances. Data show that ETU concentrates on processing. Additional residue date are required.

Toxicology Data. The toxicology data are insufficient to determine an Acceptable Daily Intake (ADI) or whether the toxicity observed in the studies is due to metiram or ETU.

There are no acceptable chronic studies on which to calculate an ADI, therefore, a three generation rat reproduction study has been used to calculate a Provisional ADI (PADI). Because a NOEL was not established in this study, an uncertainty factor of 1000 was employed. The PADI for metiram is 0.0003 mg/kg/day.

The theoretical maximum residue contribution (TMRC), based on the assumption that 100 percent of each crop is treated and contain residues at the tolerance level, is 0.009 mg/kg/day or approximately 3000 percent of the PADI. Based on a more realistic dietary assessment, using anticipated residue contributions and estimated percent crop treated, the estimated average consumption for the U.S. population is 0.0004 mg/kg/day or 128 percent of the PADI.

Tolerances Issued. Currently tolerances for metiram are expressed as zinc ethylenebisdithiocarbamate equivalents, as are the tolerances for other pesticides of the dithiocarbamate class. These tolerances are set forth in 40 CFR 180.217 and 40 CFR 180.319. There are several Canadian tolerances estabished for residues of EBDC's, including metiram, as well as several Codex Alimentarius tolerances. There are no Mexican tolerances.

IV. REGULATORY POSITION AND RATIONALE

A. REGULATORY POSITIONS AND RATIONALES

Based on the review and evaluation of all available data on metiram, the Agency has made the following determinations. Where it is the Agency position that label revisions are needed in order for a product to remain in compliance with FIFRA, specific language will be set forth in Section D of this Chapter.

1. The Agency has initiated a Special Review of metiram as part of the EBDC Special Review. EPA is currently evaluating the potential human health risks resulting from the food, field and food crop, and terrestrial non-food uses of metiram and the other EBDC pesticides containing the common contaminant, degradation product, and metabolite, ETU.

   Rationale: The EBDC's were placed in Special Review in 1977 based on the presumption that the EBDC's and ETU posed potential risks to human health or the environment. The Special Review was concluded in 1982 and the EBDC's were returned to the registration process.

   In June 1987, the Agency initiated a Special Review of the EBDC pesticides because of concern about the oncogenic risk to consumers from dietary exposure to ETU from foods treated with these pesticides, and the risks of teratogenicity and adverse thyroid effects to applicators and mixer/loaders from exposure to ETU. ETU is present as part of the residue of the EBDC pesticides or their conversion on or in treated agricultural commodities. In addition, a portion of the EBDC pesticide residues converts into ETU in the body after ingestion of commodities with EBDC residues. The Special Review issues are discussed in the Background section of this document.

   ETU, a contaminant, degradation product, and metabolite of all the EBDC's, is mutagenic, oncogenic and teratogenic, and the Agency has classified it as a Group B2 oncogen (Probable Human Carcinogen). See the Agency Assessment section of this Standard for a discussion of the classification of ETU.

2. At this time the Agency will not restrict the use of metiram products to certified applicators.

   Rationale: Based on available data, metiram products have not met or exceeded any criteria specified in 40 CFR 152.170 which would indicate a need to restrict the use of metiram to certified applicators. However, additional data have recently been received and are being reviewed. Once the data are reviewed, the Agency will make a determination regarding restricted use for metiram and the other EBDC's.

3. The Agency will not consider establishment of any new food use tolerances for metiram.

   Rationale: The current residue chemistry and toxicology data are not sufficient to assess existing and pending tolerances. The toxicology data base is insufficient to determine an ADI and also does not allow a decision as to whether observed toxicity is due to metiram or ETU. Using anticipated residues, dietary exposure currently is 128% of the preliminary ADI. Moreover, the anticipated dietary exposure to ETU from metiram use alone is 98% of the preliminary ADI. Although this percentage may be adjusted downward as additional data become available, the ETU dietary contribution from other EBDC's has not been included.

4. The Agency will consider the need for establishment of tolerances for ETU and any intermediate metabolites when data are sufficient to permit such decisions.

   Rationale: The toxicology data base for metiram is insufficient to determine whether observed toxicity is due to metiram, ETU, or additional metabolites.

5. The Agency will not establish any food/feed additive regulations pursuant to Section 409 of the Federal Food, Drug and Cosmetic Act (FFDCA).

   Rationale: The Delaney Clause in Section 409 of the FFDCA bars the establishment of food additive regulations for substances which induce cancer in man or test animals, with certain exceptions. The Agency is currently developing a position relative to the Delaney Clause and FIFRA. Once this policy has been established, the Agency will determine what action is required in relation to pesticides which have produced positive oncogenic responses in chronic animal studies.

6. Metiram is currently registered for use on peanut foliage. The Agency is requiring a tolerance and supporting data for residues on peanut hulls.

Rationale: A tolerance has not been established for peanut hulls in which residues of metiram could occur. The registrant(s) must propose a tolerance and provide supporting data.

7. Protective clothing labeling for metiram products, as stipulated as a result of the 1982 Decision Document, should be updated as noted herein in order to remain in compliance with FIFRA.

   Rationale. A major toxicological concern from exposure to metiram at this time is the hazard to the human thyroid from the degradation product, ETU, an acknowledged goitrogen, teratogen, and oncogen. Additional data are required to determine whether metiram also poses a teratogenic risk. The Agency believes that risks of teratogenicity and thyroid toxicity to commercial applicators can be reduced by maintaining the requirement that protective clothing be worn while mixing, loading and applying the chemical. The Agency believes that the same is true for other agricultural mixers, loaders, and applicators. Updated labeling statements are given in Chapter IV. D.

8. In order to remain in compliance with FIFRA, the importance of observing the preharvest intervals must be highlighted on labels of residential (homeowner) products. Language is specified Chapter IV. D.

   Rationale. In the 1982 Decision Document, the Agency determined that, as a risk reduction measure to reduce human dietary exposure, preharvest intervals must be highlighted on residential labels so that home garden users will be encouraged to comply with them. Although the risks from dietary exposure to metiram cannot be fully assessed at this time, the Agency believes continuation of this emphasis as a risk reduction measure is warranted. Specific language has been chosen to emphasize to users the importance of adherence to the preharvest intervals.

9. The Agency is requiring reentry data for metiram. In order to remain in compliance with FIFRA, an interim 24-hour reentry interval requirement must be placed on the labels of all metiram end-use products registered for agricultural use, until the required data are submitted and evaluated and any change in this reentry interval is announced.

   Rationale. Metiram meets both the chronic toxicity and exposure criteria specified in 40 CFR 158.140 for reentry data. Until these data are received and evaluated, an interim 24-hour reentry interval will serve to reduce exposure of field workers to this chemical.

10. The Agency will evaluate the potential of metiram to contaminate ground water after it has received and

evaluated additional required environmental fate data. Special ground water monitoring studies are being required.

Rationale. Metiram was identified as a chemical with the potential to contaminate ground water and a Data Call In was issued. Results of the studies received were inconclusive, but, they demonstrate that ETU has the potential to leach. Additional data are required to fully assess the potential of metiram and ETU from the use of metiram to contaminate ground water.

11. The Agency is not specifying endangered species labeling at this time.

    Rationale: A risk assessment of metiram is deferred until the Agency has reviewed fish and wildlife toxicity data which have recently been submitted to the Agency. Once the data are reviewed, the Agency may need to consult with the U.S. Fish and Wildlife Service. Endangered species labeling may then be necessary in the future based on the results of the studies and this consultation.

12. The Agency is requiring analysis of metiram to determine whether nitrosamines may be formed.

    Rationale: There is a possibility for the formation of nitrosamines during the manufacture of metiram; however, the Agency does not have adequate data to determine whether nitrosamines may be formed.

13. The Agency has determined that all data will be immediately reviewed as they are submitted.

    Rationale: Because of the general concerns over ETU and the EBDC's, the Agency believes it is essential that these data be reviewed as they are received.

14. While data gaps are being filled, currently registered manufacturing-use products (MP's) and end-use products (EP's) containing metiram as the sole active ingredient may be sold, distributed, formulated, and used, subject to the terms and conditions specified in this Standard. However, new uses will not be registered. Registrants must provide or agree to develop and provide additional data, as specified in the Data Appendices, in order to maintain existing registrations.

    Rationale: Under FIFRA, the Agency may elect not to cancel or withhold registration even though data are missing or are inadequate (see FIFRA section 3(c)(2)(B) and 3(c)(7)). Issuance of this Standard provides a mechanism for identifying data needs. These data will be reviewed and evaluated, after which the Agency will determine if additional regulatory changes are necessary. The Agency will not consider registration of any new uses while data gaps are being filled and data evaluated, based on its concerns for metiram and ETU as explained herein.

B. CRITERIA FOR REGISTRATION

To be registered or reregistered under this Standard, products must contain metiram as the sole active ingredient, bear specified labeling, and conform to the product composition, acute toxicity limits, and use pattern requirements listed in this section.

C. ACCEPTABLE RANGES AND LIMITS

Product Composition Standard - To be registered or reregistered under this Standard, manufacturing-use products (MP's) must contain metiram as the sole active ingredient. Each MP formulation proposed for registration must be fully described with an appropriate certification of limits, stating maximum and minimum amounts of the active ingredient and inert ingredients which are present in products, as well as impurities found at greater than 0.1% and any N-nitroso compounds at greater than 1 ppm.

Acute Toxicity Limits - The Agency will consider registration of technical grade and manufacturing-use products containing metiram provided that the product labeling bears appropriate precautionary statements for the acute toxicity category in which each product is placed.

Use Patterns - To be registered under this Standard, manufacturing-use products must be labeled for formulation into other manufacturing-use products or into end-use products bearing federally registered uses. The use Index (EPA Compendium of Acceptable Uses) (for availability see page 7) lists all federally-registered uses of metiram, as well as approved maximum application rates and frequencies.

D. LABELING

All metiram products must bear appropriate labeling as specified in 40 CFR 156.10. Appendix II contains additional information on labeling.

In order to remain in compliance with FIFRA, no pesticide product containing metiram may be released for shipment by the registrant after November 1, 1989, unless the product bears an amended label which complies with the specifications of this Standard.

In order to remain in compliance with FIFRA, no pesticide product containing metiram may be distributed, sold, offered for sale, held for sale, shipped, delivered for shipment, or received and (having been so received) delivered or offered to be delivered by any person after November 1, 1990, unless the product bears an amended label which complies with the specifications of this Standard.

In addition to the above, in order to remain in compliance with FIFRA, the following information must appear on the labeling:

1. Ingredient Statement. The ingredient statement for MP's and EP's must list the active ingredient as:

   A mixture of 5.2 parts by weight (83.9%) of ammoniates of [ethylenebis(dithiocarbamato)]-zinc with 1 part by weight (16.1%) ethylenebis=[dithiocarbamic acid] bimolecular and trimolecular cyclic anhydrosulfides and disulfides............(%)

   Inert Ingredients................................(%)

2. Use Pattern Statements. All manufacturing-use products must state that they are intended for formulation into end-use products only for acceptable use patterns. However, no use may be included on the label where the registrant fails to agree to comply with the data requirements in Table A for that use pattern.

3. Disposal Statements. Because metiram has not been designated as an acute or toxic hazardous waste under the Resource Conservation and Recovery Act (RCRA), the following is the appropriate pesticide disposal statement for metiram products:

   > "Wastes resulting from the use of this product may be disposed of on site or at an approved waste disposal facility."

   The labels of all products must bear the appropriate container disposal statement (See Appendix II).

4. Precautionary Statements

   Manufacturing-Use Products

   "This pesticide is toxic to fish. Do not discharge effluent containing this product into lakes, streams, ponds, estuaries, oceans, or public water unless this product is specifically identified and addressed in an

NPDES permit. Do not discharge effluent containing this product to sewer systems without previously notifying the sewage treatment plant authority. For guidance, contact your State Water Board or Regional Office of the EPA."

End-Use Products

a. Agricultural Use Products

"This pesticide is toxic to fish. Drift and runoff from treated areas may be hazardous to aquatic organisms in neighboring areas. Do not apply directly to water or wetlands (swamps, bogs, marshes, and potholes). Do not contaminate water when disposing of equipment washwaters."

All Home Use Products

> "PROTECTIVE MEASURES: Always spray with your back to the wind. Wear long-sleeve shirt, long pants, and rubber gloves. Wash gloves thoroughly with soap and water before removing. Change your clothes immediately after using this product and launder separately from other laundry items before reuse. Shower immediately after use."

Home Use Products with Food Uses

> "Preharvest intervals on this label are specified so that pesticide residues will be at an acceptable level when the crop is harvested."

All Agricultural Products

> "After (sprays have dried or dusts have settled as applicable) do not enter or allow entry into treated areas or areas where there is a danger of drift until the 24-hour reentry interval has expired unless wearing the personal protective equipment listed on the label."
>
> "Keep all unprotected persons, children, livestock, and pets away from treated area or where there is danger of drift."
>
> "Do not rub eyes or mouth with hands. See First Aid (Practical Treatment Section)."

"PERSONAL PROTECTIVE EQUIPMENT

HANDLERS (MIXERS, LOADERS, AND APPLICATORS) AND EARLY REENTRY WORKERS MUST WEAR THE FOLLOWING PROTECTIVE CLOTHING AND EQUIPMENT: a long-sleeve shirt and long pants or a coverall; chemical resistant gloves, shoes, socks, and goggles or a face shield. During mixing and loading, a chemical resistant apron must also be worn.

During application from a tractor with a completely enclosed cab with positive pressure filtration, or aerially with an enclosed cockpit, a long-sleeve shirt and long pants may be worn in place of the above protective clothing. Chemical resistant gloves must be available in the cab or cockpit and worn while exiting.

IMPORTANT! Before removing gloves, wash them with soap and water. Always wash hands, face, and arms with soap and water before eating, smoking or drinking. Always wash hands and arms with soap and water before using the toilet.

After work take off all clothes and shoes. Shower using soap and water. Wear only clean clothes. Do not use contaminated clothing. Wash protective clothing and protective equipment with soap and water after each use. Personal clothing worn during use must be laundered separately from household articles. Clothing and protective equipment drenched with metiram must be destroyed according to state and local regulations.

DRENCHED CLOTHING CANNOT BE ADEQUATELY DECONTAMINATED.

During aerial application, human flaggers are prohibited unless in totally enclosed vehicles."

Grazing Statements - As appropriate, the following grazing statements must appear on EP labels containing metiram:

° For apples, pecans:

"Do not graze livestock on treated areas"

° For corn (sweet):

"Do not feed forage to livestock"

- For cotton:

  "Do not graze treated fields or feed gin trash to dairy or meat animals"

- For peanuts:

  "Do not feed treated forage to dairy or meat animals"

- For sugar beets:

  "Do not feed treated tops to dairy or meat animals"

- For potato (seed pieces):

  "Do not use treated seed pieces for food or feed purposes"

- For asparagus

  "Do not harvest during season of application"

V. PRODUCTS SUBJECT TO THIS STANDARD

All products containing one or more of the pesticides identified in Section II.A. are subject to certain requirements for data submittal or changes in composition, labeling or packaging of the product. The applicable requirements depend on whether the product is a manufacturing or end use product and whether the pesticide is the sole active ingredient or one of multiple active ingredients.

Products are subject to this Registration Standard as follows:

A. Manufacturing use products containing this pesticide as the sole active ingredient are subject to:

1. The restrictions (if any) upon use, composition, or packaging listed in Section IV, if they pertain to the manufacturing use product.
2. The data requirements listed in Tables A and B[2]
3. The labeling requirements specified for manufacturing use products in Section IV.
4. Administrative requirements (application forms, Confidential Statement of Formula, data compensation provisions) associated with reregistration.

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[2] Data requirements are listed in the three Tables in Appendix I of this Registration Standard. The Guide to Tables in that Appendix explains how to read the Tables.

Table A lists generic data requirements applicable to all products containing the pesticide subject to this Registration Standard. Table B lists product-specific data applicable to manufacturing use products. The data in Tables A and B need not be submitted by an end use producer who is eligible for the generic data exemption for that active ingredient.

Table C lists product-specific data applicable to end use products. The Agency has decided that, in most cases, it will not require the submittal of product-specific data for end use products at this time. Therefore most Registration Standards do not contain a Table C.

B. Manufacturing use products containing this pesticide as one of multiple active ingredients are subject to:

1. The data requirements listed in Table A.

2. The labeling requirements specified for manufacturing use products in Section IV.

C. End use products containing this pesticide as the sole active ingredient are subject to:

1. The restrictions (if any) upon use, composition, or packaging listed in Section IV if they pertain to the end use product.

2. If eligible for the generic data exemption[3], the data requirements listed in Table C.

3. If not eligible for the generic data exemption, the data requirements listed in Table A and the data requirements listed in Table C.

4. The labeling requirements specified for end use products in Section IV.

D. End use products containing this pesticide as one of multiple active ingredients are subject to:

1. If not eligible for the generic data exemption, the data requirements listed in Tables A and C.

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[3] If you purchase from another producer and use as the source of your active ingredient only EPA-registered products, you are eligible for the generic data exemption for generic data concerning that active ingredient (Table A) and product-specific data for the registered manufacturing use product you purchase (Table B).

Two circumstances nullify this exemption:

1) If you change sources of active ingredient to an unregistered product, formulate your own active ingredient, or acquire your active ingredient from a firm with ownership in common with yours, you individually lose the exemption and become subject to the data requirements in Table A.

2) If no producer subject to the generic data requirements in Table A agrees to submit the required data, all end use producers lose the exemption, and become subject to the data requirements in Table A.

2. If eligible for the generic data exemption, the data requirements listed in Table C.

3. The labeling requirements specified for end use products in Section IV.

VI. REQUIREMENT FOR SUBMISSION OF GENERIC DATA

This portion of the Registration Standard is a notice issued under the authority of FIFRA sec. 3(c)(2)(B). It refers to the data listed in Table A, which are required to be submitted by registrants to maintain in effect the registration of products containing this active ingredient.[4]

A. What are generic data?

Generic data pertain to the properties or effects of a particular active ingredient. Such data are relevant to an evaluation of all products containing that active ingredient regardless of whether the product contains other ingredients (unless the product bears labeling that would make the data requirement inapplicable).

Generic data may also be data on a "typical formulation" of a product. "Typical formulation" testing is often required for ecological effects studies and applies to all products having that formulation type. These are classed as generic data, and are contained in Table A.

B. Who must submit generic data?

All current registrants are responsible for submitting generic data in response to a data request under FIFRA sec. 3(c)(2)(B) (DCI Notice). EPA has decided, however, not to require a registrant who qualifies for the formulator's exemption (FIFRA sec. 3(c)(2)(D) and § 152.85) to submit generic data in response to a DCI notice if the registrant who supplies the active ingredient in his product is complying with the data request.

If you are granted a generic data exemption, you rely on the efforts of other persons to provide the Agency with the required data. If the registrants who have committed to generate and submit the required data fail to take appropriate steps to meet the requirements or are no longer in compliance with this data requirements notice, the Agency will consider that both they and you are not in compliance and will normally initiate proceedings to suspend the registrations of both your product(s) and their product(s) unless you commit to submit and submit the required data in the specified timeframe. In such cases, the Agency generally will not grant a time extension for submitting the data.

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[4] Registrations granted after issuance of this Standard will be conditioned upon submittal or citation of the data listed in this Registration Standard.

If you are not now eligible for a generic data exemption, you may qualify for one if you change your source of supply to a registered source that does not share ownership in common with your firm. If you choose to change sources of supply, the Confidential Statement of Formula must identify the new source(s) and you must submit a Generic Data Exemption Statement.

If you apply for a new registration for products containing this active ingredient after the issuance of this Registration Standard, you will be required to submit or cite generic data relevant to the uses of your product if, at the time the application is submitted, the data have been submitted to the Agency by current registrants. If the required data have not yet been submitted, any new registration will be conditioned upon the new registrant's submittal or citation of the required data not later than the date upon which current registrants of similar products are required to provide such data. See FIFRA sec. 3(c)(7)(A). If you thereafter fail to comply with the condition of that registration to provide data, the registration may be cancelled (FIFRA sec. 6(e)).

C. What generic data must be submitted?

You may determine which generic data you must submit by consulting Table A. That table lists the generic data needed to evaluate current uses of all products containing this active ingredient, the uses for which such data are required, and the dates by which the data must be submitted to the Agency.

D. How to comply with DCI requirements.

Within 90 days of your receipt of this Registration Standard, you must submit to EPA a completed copy of the form entitled "FIFRA Section 3(c)(2)(B) Summary Sheet" (EPA Form 8580-1, enclosed) for each of your products. On that form you must state which of the following six methods you will use to comply with the DCI requirements:

1. You will submit the data yourself.

2. You have entered into an agreement with one or more registrants to jointly develop (or share in the cost of developing) the data, but will not be submitting the data yourself. If you use this method, you must state who will

submit the data on which you will rely. You must also provide EPA with documentary evidence that an agreement has been formed which allows you to rely upon the data to be submitted. Such evidence may be: (1) your letter offering to join in an agreement and the other registrant's acceptance of your offer, (2) a written statement by the parties that an agreement exists, or (3) a written statement by the person who will be submitting the data that you may rely upon its submittal. The Agency will also require adequate assurance that the person whom you state will provide the data is taking appropriate steps to secure it. The agreement to produce the data need not specify all of the terms of the final arrangement between the parties or a mechanism to resolve the terms.

If you and other registrants together are generating or submitting requested data as a task force or consortium, a representative of the group should request a Joint Data Submitter Number, as part of your 90-day response. The request must include the following information:

a. A list of the members of the consortium;
b. The name and address of the designated representative of the consortium, with whom EPA will correspond concerning the data;
c. Identity of the Registration Standard containing the data requirement;
d. A list of the products affected (from all members of the consortium); and
e. Identification of the specific data that the consortium will be generating or submitting.

The Agency will assign a number to the consortium, which should be used on all data submittals by the consortium.

3. You have attempted to enter into an agreement to jointly develop data, but no other registrant has accepted your offer. You request that EPA not suspend your registration for non-compliance with the DCI. EPA has determined that, as a general policy, it will not suspend the registration of a product when the registrant has in good faith sought and continues to seek to enter into a data development/cost sharing program, but the other registrants developing the data have refused to accept its offer. [If your offer is accepted, you may qualify for Option 2 above by entering into an agreement to supply the data.]

In order to qualify for this method, you must:

1. File with EPA a completed "Certification of Attempt to Enter into an Agreement with other Registrants for Development of Data" (EPA Form 8580-6, enclosed).

2. Provide us with a copy of your offer to the other registrant and proof of the other registrant's receipt of your offer (such as a certified mail receipt). Your offer must, at a minimum, contain the following language or its equivalent:

> [Your company name] offers to share in the burden of producing the data required pursuant to FIFRA sec. 3(c)(2)(B) in the [name of active ingredient] Registration Standard upon terms to be agreed or failing agreement to be bound by binding arbitration as provided by FIFRA section 3(c)(2)(B)(iii).

The remainder of your offer may not in any way attempt to limit this commitment. If the other registrant to whom your offer is made does not accept your offer, and if the other registrant informs us on a DCI Summary Sheet that he will develop and submit the data required under the DCI, then you may qualify for this option. In order for you to avoid suspension under this method, you may not later withdraw or limit your offer to share in the burden of developing the data.

In addition, the other registrant must fulfill its commitment to develop and submit the data as required by this Notice in a timely manner. If the other registrant fails to develop the data or for some other reason would be subject to suspension, your registration as well as that of the other registrant will normally be subject to initiation of suspension proceedings, unless you commit to submit and submit the required data in the specified timeframe. In such cases, the Agency generally will not grant a time extension for submitting the data.

4. You request a waiver of the data requirement. If you believe that a data requirement does not (or should not) apply to your product or its uses, you must provide EPA with a statement of the reasons why you believe this is so. Your statement must address the specific composition or use factors that lead you to believe that a requirement does not apply. Since the Agency has carefully considered the composition and uses of pesticide products in determining that a data requirement applies, EPA does not anticipate that many waivers will be granted. A request for waiver does not extend the timeframes for developing required data, and if your waiver request is denied, your registration may be suspended if you fail to submit the data. The Agency will respond in writing to your request for a waiver.

5. You request that EPA amend your registration by deleting the uses for which the data are needed. You are not required to submit data for uses which are no longer on your label.

6. You request voluntary cancellation of the registration of your product(s) for which the data are needed.

E. Regiscrant Requests Regarding Data Requirements and Agency Responses

All requests for modification of data requirements (inapplicability, waiver), approval of protocols or protocol changes, or time extensions must be submitted in writing. The original requirement remains in effect unless the Agency has notified you in writing that it has agreed to a change in the requirement. While being considered by the Agency, such requests for changes in the requirements do not alter the original requirements or extend the time allowed for meeting the requirement.

F. Test Protocols and Standards

All studies required under this Notice must be conducted in accordance with test standards outlined in the Pesticide Assessment Guidelines, unless other protocol or standards are approved for use by the Agency in writing. All testing must be conducted in accordance with applicable Good Laboratory Practices regulations in 40 CFR Part 160.

The Pesticide Assessment Guidelines, which are referenced in the Data Tables, are available from the National Technical Information Service (NTIS), Attn: Order Desk, 5285 Port Royal Road, Springfield, VA 22161 (tel: 703-487-4650).

Protocols approved by the Organization for Economic Cooperation and Development (OECD) are also acceptable if the OECD-recommended test standards conform to those specified in the Pesticide Data Requirements regulation (Part 158.70). Please note, however, that certain OECD standards (such as test duration, selection of test species, and degradate identification which are environmental fate requirements) are less restrictive than those in the EPA Assessment Guidelines listed above. When using the OECD protocols, they should be be modified as appropriate so that the data generated by the study will satisfy the requirements of Part 158. Normally, the Agency will not extend deadlines for complying with data requirements when the studies were not conducted in accord with acceptable standards. The OECD protocols are available from OECD, 1750 Pennsylvania Avenue, N.W., Washington, D.C. 20006.

G. Procedures for requesting a change in test protocol.

If you will generate the required data and plan to use test procedures which deviate from EPA's Pesticide Assessment Guidelines or the Reports of Expert Groups to the Chemicals Group, Organization for Economic Cooperation and Development (OECD) Chemicals Testing Programme, you must submit for EPA approval the protocols you propose to use.

You should submit your protocols before beginning testing, because the Agency will not ordinarily accept as sufficient studies using unapproved protocols. A request for protocol approval will not extend the timeframe for submittal of the data, nor will extensions generally be given to conduct studies due to submittal of inappropriate protocols. The Agency will respond in writing to your request for protocol approval or change.

H. Procedures for requesting extensions of time.

If you think that you will need more time to generate the data than is allowed by EPA's schedule, you may submit a request for an extension of time.

EPA will view failure to request an extension before the data submittal response deadline as a waiver of any future claim that there was insufficient time to submit the data. While EPA considers your request, you must strive to meet the deadline for submitting the data.

The extension request should state the reasons why you believe that an extension is necessary and the steps you have taken to meet the testing deadline. Time extensions normally will not be granted due to problems with laboratory capacity or adequacy of funding, since the Agency believes that with proper planning these can be overcome. The Agency will respond in writing to any requests for extension of time.

I. Data Format and Reporting Requirements

All data submitted in response to this Notice must comply with EPA requirements regarding the reporting of data, including the manner of reporting, the completeness of results, and the adequacy of any required supporting (or raw) data, including, but not limited to, requirements referenced or included in this Notice or contained in PR Notice 86-5 (issued July 29, 1986). All studies must be submitted in the form of a final report; a preliminary report will not be considered to fulfill the submittal requirement.

J. Existing stocks provision upon suspension or cancellation.

The Agency has determined that if a registration is suspended for failure to respond to a DCI request under FIFRA sec. 3(c)(2)(B), an existing stocks provision for the registrant is not consistent with the Act. Accordingly, the Agency does not anticipate granting permission to sell or distribute existing stocks of suspended product except in rare circumstances. If you believe that your product will be suspended or cancelled and that an existing stocks provision should be granted, you have the burden of clearly demonstrating to EPA that granting such permission would be consistent with the Act. The following information must be included in any request for an existing stocks provision:

1. Explanation of why an existing stocks provision is necessary, including a statement of the quantity of existing stocks and your estimate of the time required for their sale or distribution; and

2. Demonstration that such a provision would be consistent with the provisions of FIFRA.

VII. REQUIREMENT FOR SUBMISSION OF PRODUCT-SPECIFIC DATA

Under its DCI authority, EPA has determined that certain product-specific data are required to maintain your registrations in effect. Product-specific data are derived from testing using a specific formulated product, and, unlike generic data, generally support only the registration of that product. All such data must be submitted by the dates specified in this Registration Standard.

If you have a manufacturing use product, these data are listed in Table B. If you have an end use product, the data are listed in Table C. As noted earlier, the Agency has decided that it will not routinely require product-specific data for end use products at this time. Therefore, Table C may not be contained in this Registration Standard; if there is no Table C, you are not required to submit the data at this time.

In order to comply with the product specific data requirements, you must follow the same procedures as for generic data. See Section VI.D through J. You should note, however, that product chemistry data are required for every product, and the only acceptable responses are options VI.D.1. (submit data) or VI.D.6.(cancellation of registration).

Failure to comply with the product-specific data requirements for your products will result in suspension of the product's registration.

VIII. REQUIREMENT FOR SUBMITTAL OF REVISED LABELING

FIFRA requires each product to be labeled with accurate, complete and sufficient instructions and precautions, reflecting the Agency's assessment of the data supporting the product and its uses. General labeling requirements are set out in 40 CFR 156.10 (see Appendix II - LABELING and SUMMARY). In addition, labeling language specific to products containing this pesticide is specified in Section IV.D of this Registration Standard. Responses to this Registration Standard must include draft labeling for Agency review.

Labeling must be either typewritten text on 8-1/2 x 11 inch paper or a mockup of the labeling suitable for storage in 8-1/2 x 11 files. Draft labeling must indicate the intended colors of the final label, clear indication of the front panel of the label, and the intended type sizes of the text.

If you fail to submit revised labeling as required, which complies with 40 CFR 156.10 and the specific instructions in Section IV.D., EPA may seek to cancel the registration of your product under FIFRA sec. 6.

IX. INSTRUCTIONS FOR SUBMITTAL

All submittals in response to this Registration Standard must be sent to the following address:

Office of Pesticide Programs
OPP Mailroom (TS-767C)
Environmental Protection Agency
401 M St., SW
Washington, D.C. 20460

Attn: Metiram Registration Standard

All submittals in response to this Registration Standard are non-fee items, including 90-day responses, protocols and waiver requests, data, and revised labeling. Submittals must be clearly identified as being in response to the Registration Standard. Under no circumstances may Registration Standard responses be combined with other types of filings for which fees are required.

A. Manufacturing Use Products (MUPs) containing the subject pesticide as sole active ingredient.

1. Within 90 days from receipt of this document, you must submit for each product subject to this Registration Standard:

a. Generic Data Exemption Statement (EPA Form 8580-3), if applicable, or the "FIFRA Section 3(c)(2)(B) Summary Sheet" (EPA Form 8580-1), with appropriate attachments.

b. Confidential Statement of Formula (EPA Form 8570-4).

c. Evidence of compliance with data compensation requirements of FIFRA sec. 3(c)(1)(D). Refer to 40 CFR 152.80-152.99.

2. Within 9 months from receipt of this document you must submit:

a. Application for Pesticide Registration (EPA Form 8570-1).

b. Two copies of any required product-specific data (See Table B).

c. Three copies of draft labeling, including the container label and any associated supplemental labeling.

d. Product Specific Data Report (EPA Form 8580-4).

3. Within the times set forth in Table A, you must submit all generic data, unless you are eligible for the generic data exemption. If for any reason any test is delayed or aborted so that the schedule cannot be met, immediately notify the Agency of the problem, the reasons for the problem, and your proposed course of action.

B. Manufacturing Use Products containing the subject pesticide in combination with other active ingredients.

1. Within 90 days from receipt of this document, you must submit:

a. Generic Data Exemption Statement (EPA Form 8580-3), if applicable, or the FIFRA sec. 3(c)(2)(B) Summary Sheet, with appropriate attachments (EPA Form 8580-1).

b. Confidential Statement of Formula (EPA Form 8570-4)

2. Within 9 months of receipt of this document, you must submit:

Three copies of draft labeling, including the container label and any associated supplemental labeling.

3. Within the time frames set forth in Table A, you must submit all generic data, unless you are eligible for the generic data exemption. If for any reason any test is delayed or aborted so that the schedule cannot be met, immediately

notify the Agency of the problem, the reasons for the problem, and your proposed course of action.

C. End Use Products containing the subject pesticide as sole active ingredient.

1. Within 90 days from receipt of this document, you must submit:

a. Generic data exemption Statement (EPA Form 8580-3), if applicable, or the FIFRA Section 3(c)(2)(B) Summary Sheet, with appropriate attachments (EPA Form 8580-1).

b. Confidential Statement of Formula (EPA Form 8570-4).

2. Within 9 months from receipt of this document you must submit:

a. Two copies of any product-specific data, if required by Table C.

b. Product Specific Data Report (EPA Form 8580-4), if Table C lists required product-specific data.

c. Three copies of draft labeling, including the container label and any associated supplemental labeling.

3. Within the times set forth in Table A, you must submit all generic data, unless you are eligible for the generic data exemption. If for any reason any test is delayed or aborted so that the schedule cannot be met, immediately notify the Agency of the problem, the reasons for the problem, and your proposed course of action.

D. End Use Products containing the subject active ingredient as one of multiple active ingredients

1. Within 90 days from receipt of this document, you must submit:

a. Generic data exemption Statement (EPA Form 8580-3), if applicable, or the FIFRA Section 3(c)(2)(B) Summary Sheet, with appropriate attachments (EPA Form 8580-1).

b. Confidential Statement of Formula (EPA Form 8570-4).

2. Within 9 months from the receipt of this document, you must submit:

Three copies of draft labeling, including the container label and any associated supplemental labeling.

3. Within the times set forth in Table A, you must submit all generic data, unless you are eligible for the generic data exemption. If for any reason any test is delayed or aborted so that the schedule cannot be met, immediately notify the Agency of the problem, the reasons for the problem, and your proposed course of action.

E. Intrastate Products

Applications for full Federal registration of intrastate products were required to be submitted no later than July 31, 1988. Unless an application for registration was submitted by that date, no product may be released for shipment by the producer after July 31, 1988.

APPENDIX I

GUIDE TO TABLES

Tables A and B contain listings of data requirements for the pesticides covered by this Registration Standard.

Table A contains generic data requirements that apply to the pesticide in all products, including data requirements for which a "typical formulation" is the test substance.

Table B contains product-specific data requirements that apply only to a manufacturing use product.

The data tables are generally organized according to the following format:

1. Data Requirement (Column 1). The data requirements are listed in the order in which they appear in 40 CFR Part 158. The reference numbers accompanying each test refer to the test protocols set out in the Pesticide Assessment Guidelines, which are available from the National Technical Information Service, 5285 Port Royal Road, Springfield, VA 22161.

2. Test Substance (Column 2). This column lists the composition of the test substance required to be used for the test, as follows:

TGAI = Technical grade of the active ingredient
PAI = Pure active ingredient
PAIRA = Pure active ingredient, radio labeled
TEP = Typical end use formulation
MP = Manufacturing use product
EP = End use product

Any other test substances, such as metabolites, will be specifically named in Column 2 or in footnotes to the table.

3. Use pattern (Column 3). This column indicates the use patterns to which the data requirement applies. Use patterns are the same as those given in 40 CFR Part 158. The following letter designations are used for the given use patterns:

A = Terrestrial, food
B = Terrestrial, non-food
C = Aquatic, food
D = Aquatic, non-food
E = Greenhouse, food
F = Greenhouse, non-food
G = Forestry
H = Domestic outdoor
I = Indoor

Any other designations will be defined in a footnote to the table.

4. Does EPA have data? (Column 4). This column indicates one of three answers:

> YES - EPA has data in its files that satisfy this data requirement. These data may be cited by other registrants in accordance with data compensation requirements of Part 152, Subpart E.
>
> PARTIALLY - EPA has some data in its files, but such data do not fully satisfy the data requirement. In some cases, the Agency may possess data on one of two required species, or may possess data on one test substance but not all. The term may also indicate that the data available to EPA are incomplete. In this case, when the data are clarified, or additional details of the testing submitted by the original data submitter, the data may be determined to be acceptable. If this is the case, a footnote to the table will usually say so.
>
> NO - EPA either possesses no data which are sufficient to fulfill the data requirement, or the data which EPA does possess are flawed scientifically in a manner that cannot be remedied by clarification or additional information.

5. Bibliographic citation (Column 5). If the Agency has acceptable data in its files, this column lists the identifying number of each study. This normally is the Master Record Identification (MRID) number, but may be a GS number if no MRID number has been assigned. Refer to the Bibliography Appendices for a complete citation of the study.

6. Must additional data be submitted? (Column 6). This column indicates whether the data must be submitted to the Agency. If column 3 indicates that the Agency already has data, this column will usually indicate NO. If column 3 indicates that the Agency has only partial data or no data, this column will usually indicate YES. In some cases, even though the Agency does not have the data, EPA will not require its submission because of the unique characteristics of the chemical; because data on another chemical can be used to fulfill the data requirement; or because the data requirement has been waived or reserved. Any such unusual situations will be explained in a footnote to the table.

7. Timeframe for submission (Column 7). If column 5 requires that data be submitted, this column indicates when the data are to be submitted, based on the issuance date of the Registration Standard. The timeframes are those established either as a result of a previous Data Call-In letter, or standardized timeframes established by PR Notice 85-5 (August 22, 1985).

8. Footnotes (at the end of each table). Self-explanatory.

TABLE A
GENERIC DATA REQUIREMENTS FOR TECHNICAL GADE OF THE ACTIVE INGREDIENT METIRAM

Data Requirement	Composition[1]	Does EPA Have Data?	Bibliographic Citation	Must Additional Data be be Submitted?	Time Frame for[4] Submission
Part 158 Subpart C - Product Chemistry					
Product Identity and Composition:					
61-2 Description of Beginning Materials and Manufacturing Process	TGAI	Yes	40507102	No	
61-3 - Discussion of Formation of Impurities	TGAI	Yes	40507102	No	
Analysis and Certification of Product Ingredients					
62-1 - Preliminary Analysis of Product Samples	TGAI	Partially	40507102	Yes[2/]	4/88[5/6/]
Physical and Chemical Characterists					
63-2 - Color	TGAI	Yes	00149526	No	
63-3 - Physical State	TGAI	Yes	00149526	No	
63-4 - Odor	TGAI	Yes	00149526	No	
63-5 - Melting Point	TGAI	Yes	00149526	No	
63-6 - Boiling Point	TGAI	N/A	N/A	No[3/]	

TABLE A
GENERIC DATA REQUIREMENTS FOR METIRAM

Data Requirement	Composition[1]	Does EPA Have Data?	Bibliographic Citation	Must Additional Data be be Submitted?	Time Frame for[4] Submission
Part 158					
Subpart C - Product Chemistry (Continued)					
Physical and Chemical Characteristics					
(Continued)					
63-7 - Density, Bulk Density, or Specific Gravity	TGAI	Yes	00149526	No	
63-8 - Solubility	TGAI or PAI	Yes	40507102 40507101	No	
63-9 - Vapor Pressure	TGAI or PAI	Yes	00149526	No	
63-10 - Dissociation Constant	TGAI or PAI	Yes	40507102	No	
63-11 - Octanol/Water Partition Coefficient	PAI	Yes	00157997	No	
63-12 - pH	TGAI	Yes	00149526	No	
63-13 - Stability	TGAI	Yes	00149526	No	
Other Requirements:					
64-1 - Submittal of samples	N/A	N/A		No	

1/ TGAI = technical grade of the active ingredient. PAI = purified active ingredient

2/ Five or more representative samples of the unregistered 89% T must be analyzed for the amount of active ingredient using a method capable of differentiating metiram from interfering CS_2-liberating impurities. If the CS_2-liberation and metiram specific methods yield different results, the CS_2-liberating impurities must be quantified. Also, complete validation data (accuracy and precision) must be submitted for each analytical method used in generating previously submitted preliminary analysis data for impurities in the 89% technical.

3/ Data are not required because the technical product is a solid at room temperature.

4/ These data have previously been requested in the Comprehensive Data Call In Notice issued April 1987. The time frame for submission of data is the same as required in the April 1987 Data Call In Notice.

5/ Data recently submitted and are being reviewed.

6/ All nitrosamines must be identified and quantified in six samples; two samples of each must be analyzed shortly after production, 3 months after production and 6 months after production. A method sensitive to 1 ppm of N-nitroso contaminants must be used.

TABLE A
GENERIC DATA REQUIREMENTS FOR METIRAM

Data Requirement	Test Substance[1]	Does EPA Have Data?	Bibliographic Citation[2]	Must Additional Data be Submitted?	Time Frame for Submission[3]
§158.240 Residue Chemistry					
171-3 - Directions for Use	---			Yes[14/]	
171-4 - Nature of Residue (Metabolism)					
- Plants	PAIRA	Partially	00088894 00160789 00160790	Yes[4/]	10/88
- Livestock	PAIRA and Plant metabolites	Partially	00088894 00157034 00160534 00161338	Yes[5/]	10/88
171-4 - Residue Analytical Method	TGAI and Metabolites	Partially	00063821 00098644 00098677 00098685 00098689 00157032 00157033 00160639 00160784 00160785 00160786 00161939	Yes[6/][7/]	15 Months
171-4 - Storage Stability	TEP or PAI, & Metabolites	No		Yes[8/][9/]	10/88

TABLE A
GENERIC DATA REQUIREMENTS FOR METIRAM

Data Requirement	Test Substance[1]	Does EPA Have Data?	Bibliographic Citation[2]	Must Additional Data be Submitted?	Time Frame for[3] Submission
§158.240 Residue Chemistry (continued)					
171-4 - Magnitude of the Residue-Residue Studies for Each Food Use 10/					
- Crop Group #1 - Root and Tuber Vegetables					
o Crop 1 - Potatoes					
-- Crop field trials	TEP	No		Yes 11/	10/88
-- Processed Food/Feed	EP	No		Yes 12/	4/89
° Crop 2 - Sugar Beet Roots					
-- Crop field trials	TEP	No		Yes 13/ 14/	10/88
-- Process Food/Feed	EP	No		Yes 15/	4/89
- Crop Group #2 - Leafy Vegetables					
° Crop 1 - Celery					
-- Crop field Trials	TEP	No		Yes 16/	10/88

TABLE A
GENERIC DATA REQUIREMENTS FOR METIRAM

Data Requirement	Test Substance[1]	Does EPA Have Data?	Bibliographic Citation[2]	Must Additional Data be Submitted?	Time Frame for[3] Submission
§158.240 Residue Chemistry (continued)					
171-4 - Magnitude of the Residue-Residue Studies for Each Food Use					
- Crop Group #3 - Fruiting Vegetables					
o Crop 1 - Tomatoes					
-- Crop field trials	TEP	No		Yes 17/	10/88
-- Processed Food/Feed	EP	No		Yes 18/	4/89
- Crop Group #4 - Cucurbits Vegetables					
o Crop 1 - Cucumbers					
-- Crop field trials	TEP	No		Yes 19/	10/88
o Crop 2 - Melons					
-- Crop field trials	TEP	No		Yes 20/	10/88
- Crop Group #5 - Pome Fruits					
o Crop 1 - Apples					
-- Crop field trials	TEP	No		Yes 21/ 22/	10/88
-- Processed Food/Feed	EP	No		Yes 23/	4/89

TABLE A
GENERIC DATA REQUIREMENTS FOR METIRAM

Data Requirement	Test Substance[1]	Does EPA Have Data?	Bibliographic Citation[2]	Must Additional Data be Submitted?	Time Frame for[3] Submission
§158.240 Residue Chemistry (continued)					
171-4 - Magnitude of the Residue-Residue Studies for Each Food Use					
- Crop Group #6 - Tree Nuts Group					
o Crop 1 - Pecans					
-- Crop field trials	TEP	No		Yes[24]	10/88
- Crop Group #7 - Cereal Grains					
o Crop 1 - Corn, fresh					
-- Crop field trials	TEP	No		Yes[25]	10/88
- Crop Group #8 - Miscellaneous Commodities					
o Crop 1 - Asparagus					
-- Crop field trials	TEP	No		Yes[26]	10/88
o Crop 2 - Peanuts					
-- Crop field trials	TEP	No		Yes[27/28/29]	10/88
-- Processed Food/Feed	EP	No		Yes[30]	4/89

TABLE A
GENERIC DATA REQUIREMENTS FOR METIRAM

Data Requirement	Test Substance[1]	Does EPA Have Data?	Bibliographic Citation[2]	Must Additional Data be Submitted?	Time Frame for[3] Submission
§158.240 Residue Chemistry (continued)					
171-4 - Magnitude of the Residue-Residue Studies for Each Food Use					
o Crop 3 - Tobacco					
-- Crop field trials	TEP	No		Yes[31/][32/]	10/88
-- Processed Food/Feed	EP	No		Yes[33/]	4/89
171-4 - Magnitude of the Residue in Meat/Milk/Poultry/Eggs	TGAI or Plant Metabolites	No		Reserved[34/]	

1/ Test Substance: TGAI = Technical grade of the active ingredient; PAIRA = Pure active ingredient, radiolabeled; TEP = Typical end-use product; PAI = Pure active ingredient.

2/ The references cited here include only those MRIDs that contain data considered partially useful for fulfillment of data requirements for plant and animal metabolism and residue analytical methods.

3/ Data must be submitted according to due dates estabished in the previous Data Call In Notices. When numbers of months are provided, these are new data requirements which must be fulfilled in the number of months specified from the registrant's receipt of this document.

4/ Data must be submitted depicting the uptake, distribution, and metabolism of [^{14}C]metiram in root and tuber and pome fruit crops following a foliar application. Sampling intervals through at least 21 days must be included. The identities and quantities of residues in or on mature plant parts must be determined in order to elucidate the terminal residues. Residue identities must be confirmed by a method such as GC, HPLC, and/or mass spectrometry. Data reflecting solvent extraction efficiency of metiram residues must be represented. Representative samples from these tests must also be analyzed by enforcement methods to ascertain that these methods are capable of determining all metabolites of concern.

5/ Metabolism studies utilizing ruminants and poultry in which animals must be dosed for a minimum of three days with [^{14}C]metiram at a level sufficient to make residue identification and quantification possible must be submitted. Milk and eggs must be collected twice a day during the dosing period. Animals must be sacrificed 24 hours after the final dose. The distribution and characterization of residues must be determined in

§158.240 Residue Chemistry (continued)

milk, eggs, liver, kidney, muscle, and fat. Data reflecting solvent extraction efficiency of metiram residues must also be represented. Note: Representative samples from the above-described tests must also be analyzed by current enforcement methods to ascertain the validity of these methods.

6/ A confirmatory enforcement method must be developed and validated that is capable of differentiating between EBDC fungicides as well as other contaminants that degrade to CS_2. Also, residues of ethylenethiourea (ETU), metiram per se and any other residues of concern discovered in the required plant metabolism studies in or on crop samples must be subjected to analysis by multiresidue method protocols I - IV, available from NTIS under order No. PB203734/AS. If it is determined that tolerances must be established for residues of metiram in animal commodities, these data will also be required for representative animal commodities.

7/ All residue data required in this Standard must be accompanied by a complete description of all analytical methods used in data collection along with complete method validation data (accuracy, precision, sensitivity) for each residue in/on each commodity.

8/ The Agency has considered possible validation of earlier submitted data, but has concluded that validation of existing crop residue, processing, and animal commodity samples would not be acceptable due to the highly variable and in many instances unknown conditions (e.g., ambient and freezer temperatures, sample handling, preparation and extraction parameters prior to analyses) which may have existed at the laboratories generating the residue data which were evaluated. In view of the lack of information on the storage conditions in the earlier studies and the importance of storage stability studies which accurately reflect storage conditions of the samples of the treated crop, processed food, and animal products, the Agency has concluded that frozen storage stability data on metiram and ETU must be generated concurrently with the required crop residue, processing, and animal commodity studies on these chemicals. Thus, the Agency considers all previously submitted field residue data, processing studies, and animal feeding studies as invalid. Footnotes 11-33 specifically detail all field residue and processing data for metiram. Data requirements for feeding studies will be determined on receipt of the required animal metabolism data.

9/ To support crop residue data, storage stability studies must be conducted on both weathered samples (metiram) and fortified frozen samples (metiram, metabolites and ETU) of one representative crop from each crop grouping (40 CFR 180.34) on which registered uses of metiram exist. Analyses of each crop must be conducted over a time period that includes the time interval that the raw agricultural commodity is held in frozen storage prior to the crop residue analysis. To support residue data on processed commodities, fortified storage stability data are required for all processing studies submitted to the Agency. Analyses must be conducted over a time period that includes the frozen storage of the raw agricultural commodity prior to processing and each processed commodity prior to the residue analyses. Protocols for these studies must be submitted to and approved by the Agency prior to initiating the studies.

TABLE A
GENERIC DATA REQUIREMENTS FOR METIRAM

§158.240 Residue Chemistry (continued)

(a) Storage stability data using weathered samples. Data are required on the parent compound, metiram, in which crop samples field treated with a typical end use product are frozen immediately upon harvesting. The integrity of the samples must be maintained by freezing. The samples must be analyzed for metiram on the day they arrive at the analytical laboratory, and then stored frozen and analyzed periodically for metiram during the time intervals specified in the Agency approved protocol.

(b) Storage stability data using fortified samples. Data are required on metiram, ETU, and metabolites in which a group of untreated samples of raw agricultural commodities and processed crops are fortified (spiked) with only metiram (pure active ingredient), another group of samples is fortified with only ETU, and other groups are fortified individually with each additional metabolite. Immediately after fortification, the samples fortified with metiram must be analyzed for metiram and ETU; samples fortified with ETU must be analyzed for only ETU; and samples fortified with other metabolites must be analyzed for only the metabolite with which the sample was fortified. Sample integrity must be maintained by freezing, and analyses for metiram, ETU, and metabolites must be conducted periodically during the time intervals specified in the Agency approved protocol.

(c) Storage stability data for livestock/poultry feeding studies. If cattle and poultry feeding studies are required (see footnote 34), fortified storage stability studies will be required on all animal commodities (i.e., tissues, milk and eggs) for which residue data are submitted to the Agency. Analyses must be conducted over a time period that includes the time interval that each commodity is held in frozen storage prior to residue analyses.

10/ For this Registration Standard, to ensure proper sequencing, the Registrant should complete and submit all plant metabolism data to the Agency for review prior to initiation of residue field trials and processing studies.

11/ Data must be submitted depicting residues of metiram, ETU, and other residues of concern in or on potatoes harvested immediately after the last of several foliar applications made at 5-day intervals with a WP formulation at 1.6 lb ai/A. Tests must be conducted in ID(24%), WA(16%) or OR(6%), ME(6%), ND(6%), WI(6%), and CO(5%) which together produced 69% of U.S.-grown potatoes in 1984 (preliminary figures, Agricultural Statistics, USDA, 1985). The Registrant must propose a maximum number of applications per season or a maximum seasonal application rate consistent with the data submitted.

12/ Data depicting metiram, ETU, and other residues of concern in chips, granules, and wet and dried potato peel processed from potatoes bearing measurable weathered residues must be submitted. If residue concentration occurs, appropriate food/feed additive tolerances must be proposed.

13/ Data depicting metiram, ETU, and other residues of concern in or on sugar beets following multiple foliar applications (using ground and aerial equipment) of a WP formulation at 2.4 lb ai/A, in 5-10 gal/A must be submitted. Applications must begin at the time of normal disease onset and continue at 7-day intervals. Tests must be conducted in CA(23%), ID(15%), MI(10%), and MN(20%) or ND(10%) to adequately represent ca. 80% of U.S. sugar beet production (Agricultural Statistics, 1985, p. 76).

TABLE A
GENERIC DATA REQUIREMENTS FOR METIRAM

§158.240 Residue Chemistry (continued)

14/ The registrant must propose a maximum number of seasonal applications or a maximum seasonal rate and a PHI. Required tests must reflect this maximum rate and proposed PHI.

15/ Data depicting metiram, ETU, and other residues of concern in dehydrated pulp, molasses, and refined sugar processed from sugar beets bearing measurable weathered residues must be submitted. If concentration of residues occurs, the registrant must propose appropriate food/feed additive tolerances.

16/ Data reflecting metiram, ETU, and other residues of concern in or on unstripped, untrimmed and unwashed celery harvested 14 days following the last of multiple foliar applications, at 3-day intervals, of the 80% WP formulation must be submitted. Applications must begin when plants are set in the field. Separate tests must be performed using ground and aerial equipment. The registrant must propose a maximum number of applications per season or a maximum seasonal use rate; test data must reflect this proposed maximum rate. Tests must be conducted in CA which produces 69% of the total U.S. celery crop (Agricultural Statistics, 1985, p. 154).

17/ Data depicting metiram, ETU, and other residues of concern in or on tomatoes harvested five days after the last of multiple foliar applications, at 7-day intervals, of the 80% WP formulation at 2.4 lb ai/A must be submitted. Separate tests must be performed using ground and aerial equipment. Applications must begin 10 days after field-seeded tomatoes emerge or soon after transplanting. The registrant must propose a maximum number of applications per season or a maximum seasonal use rate; required studies must reflect the proposed maximum rate. Tests must be conducted in CA(27%) and FL(50%), which collectively produce 77% of the U.S. tomatoes grown for fresh market (Agricultural Statistics, 1985, p. 172).

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18/ Data depicting metiram, ETU, and other residues of concern in wet and dry pomace, tomato juice, puree, and catsup processed from tomatoes bearing measurable, weathered residues must be submitted. Should residues concentrate in any of these processed commodities, appropriate food/feed additive tolerances must be proposed.

19/ Data depicting metiram, ETU, and other residues of concern in or on cucumbers harvested 5 days following the last of multiple foliar applications of the 80% WP formulation at 1.6 lb ai/A must be submitted. Treatments must be applied using ground and aerial equipment. The registrant must propose a maximum seasonal use rate or a maximum number of applications per season; test data must reflect the proposed maximum rate. Tests must be conducted in CA(8%), FL(4%), MI(18%), NC(14%), TX(7%), and WI(10%) which collectively produced 61% of the total U.S. cucumbers (for pickles) in 1984 (Agricultural Statistics, 1985, p. 157).

20/ Data depicting residues of metiram, ETU, and other residues of concern in or on cantaloupes harvested 5 days following the last of multiple foliar applications of the 80% WP formulation at 1.6 lb ai/A must be submitted. Applications must be made using ground and aerial equipment in separate tests. The registrant must propose a maximum seasonal use rate or a maximum number of applications per season; test data must reflect the proposed maximum rate. Tests must be conducted in CA(52%) and TX(21%) which accounted for 73% of the 1982 U.S. cantaloupe acreage (1982 Census of Agriculture, Vol. 1, Part 51, p. 339).

TABLE A
GENERIC DATA REQUIREMENTS FOR METIRAM

§158.240 Residue Chemistry (continued)

21/ Data must be submitted depicting residues of concern in/on apples harvested 15 days after the last of several foliar applications made at intervals to be specified by the Registrant using a WP formulation as follows: (i) by ground equipment, at 1.6 lb ai/100 gal to runoff [up to 12.8 lb ai/A - maximum rate currently specified on label] until petal fall followed by cover sprays at 1.2 lb ai/100 gal to runoff [up to 9.6 lb ai/A - maximum cover spray rate]; and (ii) by aerial equipment, at 6.4 lb ai/A through the first cover spray followed by 4.8 lb ai/A at the second and later cover sprays. Information regarding tree size and spacing and the number of gal/A applied must be provided for each test. Tests must be conducted in IL, PA, and VA, major apple production states where the 15-day PHI is permitted (Agricultural Statistics, USDA, 1985). [In more major production states such as WA, NY, MI and CA, the PHI is 30 days.

22/ The registrant must propose label revisions that limit the number of applications per season (or set a maximum seasonal application rate) and specify a minimum interval between applications which must be reflected by the submitted data.

23/ Data must be submitted depicting residues of metiram, ETU, and other residues of concern in wet and dry pomace and juice processed from apples bearing measurable weathered residues. If residues concentrate in juice, an appropriate food additive tolerance must be proposed. Also, an appropriate feed additive tolerance must be proposed for residues in dry pomace.

24/ Data depicting metiram, ETU, and other residues of concern in or on pecans harvested at maturity following multiple foliar applications of the 80% WP formulation must be submitted. The last application must occur at shuck split. Separate tests must be conducted using ground equipment (at 1.6 lb ai/100 gal), and aerial equipment or mist blowers (at 6.4 lb ai/A). The registrant must propose a maximum number of applications per season or a maximum seasonal use rate. Required tests must reflect the proposed maximum rate. Tests must be conducted in AZ(13%), GA(47%), and TX(14%), which produce 74% of the total U.S. pecan crop (1982 Census of Agriculture Vol. 1, Part 51, p. 368).

25/ Data must be submitted depicting residues in or on sweet corn (kernels plus cob with husks removed) harvested 1 day after the last of several foliar applications made at intervals to be specified by the Registrant using the 80% WP formulation at 3.2 lb ai/200 gal/A. The Registrant must propose label restrictions specifying the minimum interval between applications and the maximum permissible number of applications or lb ai/A/season. The submitted data must reflect these proposed restrictions. Tests must be conducted in FL, the only state in which metiram use on sweet corn is permitted.

26/ Data depicting metiram, ETU, and other residues of concern in or on asparagus harvested from plants treated with multiple postharvest foliar applications of the 80% WP formulation at 2.4 lb ai/A using both

TABLE A
GENERIC DATA REQUIREMENTS FOR METIRAM

§158.240 Residue Chemistry (continued)

ground and aerial equipment in separate tests must be submitted. The registrant must propose a maximum seasonal rate or number of applications per season which must be reflected by the submitted data. Also, the registrant must propose a label restriction against harvesting during the season of application. Tests must be conducted in CA(36%), MI(20%), and WA(31%), which collectively account for Ca. 90% of U.S. commercial asparagus production (1982 Census of Agriculture, Vol. 1, Part 51, p. 335).

27/ Data depicting metiram, its metabolite ETU, and any additional residues of concern in or on nuts and hulls from peanuts treated (using both ground and aerial equipment) with multiple foliar applications of the 80% WP at 1.6 lb ai/A and the 3.5, 5, or 7% D at 1.5 lb ai/A repeated at 10-day intervals must be submitted. Tests must be conducted in AL(15%), GA(49%), and NC(10%) to adequately represent Ca. 70% of U.S. peanut production (Agricultural Statistics, 1985, p. 121).

28/ The registrant must propose a PHI and a maximum number of applications per season or a maximum seasonal rate which must be reflected in the required data.

29/ Since peanut hulls are a raw agricultural commodity, the registrant must propose a tolerance for residues in or on peanut hulls.

30/ The registrant must submit data depicting concentration of metiram, ETU, and other residues of concern during the processing of meal, crude oil, refined oil and soapstock from treated peanuts. If concentration occurs in any of these products during processing, appropriate food/feed additive tolerances must be proposed. However, final disposition of these food/feed additive regulations is dependent upon the Agency's position regarding Delaney Clause issues.

31/ Data must be submitted depicting metiram, ETU, and other residues of concern in or on green, freshly harvested tobacco receiving the following full-season treatment schedule: multiple foliar plant bed treatment of the 80% WP formulation at 1.6 lb ai/100 gal (3-6 gal/100 sq yd) and the 3.5% D formulation at 0.14 lb ai/100 sq yd, respectively. The registrant must propose a maximum seasonal application rate or a maximum number of applications per season. Required studies must reflect these rates.

32/ Data depicting metiram, ETU, and other residues of concern in or on green, freshly harvested tobacco receiving multiple foliar applications of the 80% WP formulation in the plant bed, and in the field, at 2.4 lb ai/A must be submitted. Tests must be conducted in GA, IN, KY, OH, and SC, states in which this use is permitted under SLN registration

33/ If residues in freshly harvested green tobacco equal or exceed 0.1 ppm, data depicting residues in or on

§158.240 Residue Chemistry (continued)

dried or cured tobacco will be required. If residues in or on dried or cured tobacco equal or exceed 0.1

ppm, pyrolysis products derived from the active ingredient must be characterized and the level of residue in smoke must be quantified. ([^{14}C]Metiram must be used for identification of pyrolysis products.

34/ Presently, the nature of the residue of metiram in animals is not adequately understood. On receipt of the data required for animal metabolism, the need for, and nature of tolerances for residues of metiram in meat, milk, poultry and eggs will be assessed and, if necessary, feeding studies will be required. Also see footnote 8.

TABLE A
GENERIC DATA REQUIREMENTS FOR METIRAM

Data Requirement	Composition[1]	Use Patterns[2]	Does EPA Have Data to Satisfy This Requirement? (Yes, No or Partially?)	Bibliographic Citation	Must Additional Data be Submitted?	Time Frame for Submission[3]
§158.290 Environmental Fate						
DEGRADATION STUDIES-LAB:						
161-1 - Hydrolysis	PAIRA	A,B	Yes	00155189 00161937	No	
	ETU	A,B	Yes	40466103	No	
Photodegradation						
161-2 - In water	PAIRA	A,B	Yes	00155190 00161938	No	
	ETU	A,B,	Yes	40466102	No	
161-3 - On soil	PAIRA	A	Yes	00157031	No	
	ETU	A	Yes	40466101	No	
161-4 - In Air	PAIRA	A	No		No[4/]	
METABOLISM STUDIES-LAB:						
162-1 - Aerobic Soil	PAIRA	A,B	Yes	00155162 00155288	No	
	ETU	A,B	No		Yes	7/89
162-2 - Anaerobic Soil	PAIRA	A	Yes	00155162 00155288	No	
	ETU	A	No		Yes	7/89
162-3 - Anaerobic Aquatic	PAIRA		-		No[5/]	
162-4 - Aerobic Aquatic	PAIRA		-		No[5/]	

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GENERIC DATA REQUIREMENTS FOR METIRAM

Data Requirement	Composition[1]	Use Patterns[2]	Does EPA Have Data to Satisfy This Requirement? (Yes, No or Partially?)	Bibliographic Citation	Must Additional Data be Submitted?	Time Frame for[3] Submission
§158.290 Environmental Fate (continued)						
MOBILITY STUDIES:						
163-1 - Leaching and Adsorption/Desorption	PAIRA	A,B	Partially	00155162 00155288	Yes[6/]	4/88[11/]
	ETU	A,B	No		Yes[6/]	4/88[11/]
163-2 - Volatility (Lab)	ETU	A	No		Yes[7/]	12 Months
163-3 - Volatility (Field)	TEP	A	No		Reserved[8/]	
DEGRADATION STUDIES-FIELD:						
164-1 - Soil	TEP	A,B	Partially	00161935	Yes	7/89
	ETU	A,B	No		Yes	7/89
164-2 - Aquatic (Sediment)	TEP				No[5/]	
164-3 - Forestry	TEP				No[5/]	
164-5 - Soil, Long-term	TEP ETU	A,B A,B	No No		Yes[9/] Yes[9/]	50 Months 50 Months
ACCUMULATION STUDIES:						
165-1 - Rotational Crops (Confined)	PAIRA	A	No		Yes[6/]	7/90
165-2 - Rotational Crops (Field)	TEP	A	No		Reserved[10/]	
165-3 - Irrigated Crops	TEP				No[5/]	

TABLE A

GENERIC DATA REQUIREMENTS FOR METIRAM

Data Requirement	Composition 1	Use Patterns2	Does EPA Have Data to Satisfy This Requirement? (Yes, No or Partially?)	Bibliographic Citation	Must Additional Data be Submitted?	Time Frame for3 Submission
§158.290 Environmental Fate (continued)						
ACCUMULATION STUDIES (continued)						
165-4 - In Fish	PAIRA ETU	A,B A,B	No No		Yes 6/ Yes	4/88 12/ 12 Months
165-5 - In Aquatic Nontarget Organisms	TEP	-	-		No 5/	
Special Studies						
Small Scale Retrospective Groundwater Monitoring Study	Metiram ETU	A,B A,B	No No		Yes 13/ 13/ Yes	Protocols due 120 days Report due 36 months after Agency acceptance of protocol. Progress reports: every 6 months

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1/ Composition: TGAI = Technical Grade of the Active Ingredient, PAIRA = Pure Active Ingredient, Radiolabeled, TEP = Typical End-Use Product.

2/ Use Patterns are coded as follows: A = Terrestrial, Food Crop; B = Terrestrial, Non-Food

3/ This data has previously been requested in the Comprehensive Data Call In Notice issued April 1987. The time frame for submission of data is the same as required in the April 1987 Data Call In Notice. Where number of months are provided, these are new data requirements which must be fulfilled in the number of months specified from the registrant's receipt of this document.

4/ Metiram has low volatility. Volatility data on ETU is not available. ETU may volatilize but is unlikely to degrade in air since it does not degrade under sunlight in water and on soil.

5/ Metiram does not have aquatic or forestry use and is not applied to crops grown/harvested under flooded conditions.

6/ Data required on both metiram and ETU. Emphasis must be placed on ETU.

7/ Studies needed for ETU.

8/ Reserved pending results of laboratory volatiltiy data and review of toxicological and reentry issues.

9/ Prospective monitoring studies and field leaching studies addressing ETU and metiram are optional as replacement for the conventional long-term field dissipation study. This study would trace the movement of ETU through the soil profile in soil pore water in the vadose zone and in shallow groundwater. Interim results of this study must be submitted for assessment 6 months after the studies are initiated. Whether the registrant elects to submit the conventional long-term field dissipation study or the prospective study, an adequate study must be submitted to the Agency within 50 months from receipt of this Registration Standard.

10/ Reserved pending results of confined rotational crop study.

11/ Data has recently been submitted and is being reviewed.

12/ A waiver request is currently under review for this requirement.

13/ A small-scale retrospective ground-water monitoring study is required. Semi-annual progress reports are due six months after receipt of this Registration Standard. During the three year period, allowed for conducting and submission of this study, it is expected that 1 year will be needed to set-up the study, and the remaining 2 years will be necessary to conduct and complete the study including preparation and submission of the final report.

TABLE A
GENERIC DATA REQUIREMENTS FOR METIRAM

Data Requirement	Composition[1]	Use Patterns[2]	Does EPA Have Data to Satisfy This Requirement? (Yes, No or Partially?)	Bibliographic Citation	Must Additional Data be Submitted?	Time Frame for Submission
§158.440 Spray Drift						
201-1 - Droplet Size Spectrum		A	No		Yes	6 Months
202-1 - Drift Field Evaluation		A	No		Yes	6 Months

1/ Composition: TGAI = Technical Grade of the Active Ingredient, PAIRA = Pure Active INgredient, Radiolabeled, TEP = Typical End-Use Product...

2/ Use Patterns are coded as follows: A = Terrestrial, Food Crop

TABLE A

GENERIC DATA REQUIREMENTS FOR METIRAM

Data Requirement	Composition[1]	Use Patterns[2]	Does EPA Have Data to Satisfy This Requirement? (Yes, No or Partially?)	Bibliographic Citation	Must Additional Data be Submitted?	Time Frame for Submission[3]
§158.340 Toxicology						
ACUTE TESTING:						
81-1 - Acute Oral - Rat	TGAI	All	No		Yes	1/88 14/
81-2 - Acute Dermal	TGAI	All	No		Yes	1/88 14/
81-3 - Acute Inhalation - Rat	TGAI	All	No		Yes	1/88 14/
81-4 - Eye Irritation - Rabbit	TGAI	All	No		Yes	1/88 14/
81-5 - Dermal Irritation - Rabbit	TGAI	All	No		Yes	1/88 14/
81-6 - Dermal Sensitization - Guinea Pig	TGAI	All	No		Yes	1/88 14/
81-7 - Delayed Neurotoxicity - Hen	TGAI	All	No		No 4/	

TABLE A
GENERIC DATA REQUIREMENTS FOR METIRAM

Data Requirement	Composition[1]	Use Patterns[2]	Does EPA Have Data to Satisfy This Requirement? (Yes, No or Partially?)	Bibliographic Citation	Must Additional Data be Submitted?	Time Frame for[3] Submission
§158.340 Toxicology - Continued						
SUBCHRONIC TESTING:						
82-1 - 90-Day Feeding: - Rodent, and	TGAI	All	Partially	000126738 40290601	Yes 5/	7/88 14/
- Non-rodent (Dog)	TGAI	All	Partially	000031591	No 6/	
82-2 - 21-Day Dermal - Rabbit	TGAI	All	No		Yes 7/	4/88 14/
82-3 - 90-Day Dermal - Rabbit	TGAI	All	No		Reserved 8/	
82-4 - 90-Day Inhalation: - Rat	TGAI	All	Yes	00164083 40044701	No	
82-5 - 90-Day Neurotoxicity	TGAI		No		No 9/	
CHRONIC TESTING:						
83-1 - Chronic Toxicity: - Rodent	TGAI	All	Partially	00098449	Yes 10/	6/90 4 months
-Stability of test substance					Yes	6/90
	ETU	All	No			
- Nonrodent	TGAI	All	No		Yes 11/	6/90
	ETU	All	No		Yes	6/90

TABLE A
GENERIC DATA REQUIREMENTS FOR METIRAM

Data Requirement	Composition[1]	Use Patterns[2]	Does EPA Have Data to Satisfy This Requirement? (Yes, No or Partially?)	Bibliographic Citation	Must Additional Data be Submitted?	Time Frame for[3] Submission
§158.340 Toxicology - Continued						
83-2 - Oncogenicity:						
- Rat	TGAI	All	Partially	00098449	Yes[10]	6/90
- Mouse	TGAI	All	Partially	00030245	Yes[12]	6/90
- Histopath & Stability info.						4 months
83-3 - Teratogenicity:						
- Rat	TGAI	All	Partially	00030565	Yes[5]	7/88[14]
- Rabbit	TGAI	All	No		Yes	7/88[14]
83-4 - Reproduction	TGAI	All	No		Yes	7/90
	ETU	All	No		Yes	7/90
MUTAGENICITY TESTING						
84-2 - Gene Mutation	TGAI	All	Partially	00148682	Yes[13]	9 Months
84-2 - Chromosomal Aberration	TGAI	All	Yes	00148681 00163786	No	
84-4 - Other Mechanisms of Mutagenicity	TGAI	All	Yes	00148680 00148679 00149528	No	
SPECIAL TESTING						
85-1 - General Metabolism	PAI or PAIRA	All	Yes	00155160	No	
85-2 - Domestic Animal Safety	Choice		No		No	

TABLE A
GENERIC DATA REQUIREMENTS FOR METIRAM

Data Requirement	Composition[1]	Use Patterns[2]	Does EPA Have Data to Satisfy This Requirement? (Yes, No or Partially?)	Bibliographic Citation	Must Additional Data be Submitted?	Time Frame for[3] Submission
§158.340 Toxicology - Continued						
85-2 - Dermal (Percutaneous) Absorption - Rat	TGAI ETU	All	Yes	00155161	No	

1/ Composition: TGAI = Technical Grade Active Ingredient; PAI = Pure Active Ingredient; PAIRA = Pure Active Ingredient, Radiolabelled; Choice = Choice of several test substances determined on a case-by-case basis.

2/ The use patterns are coded as follows: A = Terrestrial, Food Crop; B = Terrestrial, Non-Food; C = Aquatic, Food Crop; D = Aquatic, Non-Food; E = Greenhouse, Non-Food; G = Forestry; H = Domestic Outdoor; I = Indoor; IP = Industrial Preservative.

3/ This data has previously been requested in the Comprehensive Data Call In Notice issued April 1987. The time frame for submission of data is the same as required in the April 1987 Notice. When number of months are provided, these are new data requirements which must be fulfilled in the number of months specified from the registrnts receipt of this document.

4/ The chemical does not belong to the organophosphate pesticides, nor is it considered to be a cholinesterase inhibitor.

5/ The available study may be upgraded to acceptable if the registrant adequately addresses the problem of stability of compound as administered. Otherwise, the study may need to be repeated.

6/ Since a chronic non-rodent study is required, further subchronic studies in non-rodents will not be required.

7/ 21-day dermal study is required before a decision can be made for the need for a longer term dermal study.

8/ Contingent upon the results of the worker exposure analysis and review of the 21-day dermal toxicity (82-2).

9/ A subchronic neurotoxicity study is not required since the acute neurotoxicity study was not required and neurotoxicity was not observed in other species.

10/ The rat study apparently did not demonstrate a maximum tolerated dose. Stability information on compound as administered will be necessary and if you elect to submit this information it must be submitted within 4 months of receipt of this document. A repeat study may be necessary if dose justification and stability information cannot be provided. An adequate oncogenicity study must be submitted to the Agency by June 1990.

11/ Special neurological observations must be added to this study. The registrant must submit a protocol within 120 days from receipt of this Registration Standard, to the Agency for consideration prior to commencing the study. [Ref: DeLahunta, A. (1983) Small animal neurologic examination and index of diseases of the nervous system. In Veterinary Neuroanatomy and Clinical Neurology, pp. 365-387. W.B. Sauders, Philadelphia.]

12/ The mouse study apparently did not demonstrate a maximum tolerated dose. Histopathology and stability information on compound as administered will be necessary. This information must be submitted to the Agency within 120 days from receipt of this document if you elect to upgrade the previous study. A repeat study may be necessary if dose justification, stability information and full histopathology information cannot be provided. An adequate oncogenicity study must be submitted to the Agency by June 1990.

13/ Marginal positive (inconclusive) results must be confirmed or refuted in a repeat assay (point mutation in CHO cells).

14/ Studies have recently been submitted and are currently being reviewed.

TABLE A
GENERIC DATA REQUIREMENTS FOR METIRAM

Data Requirement	Composition[1]	Use Pattern[2]	Does EPA Have Data To Satisfy This Requirement? (Yes, No or Partially)	Bibliographic Citation	Must Additional Data Be Submitted Under FIFRA §3(c)(2)(B)? Time Frames for Data Submission[3]	
§158.390 Reentry Protection						
132-1 - Foliar Dissipation	TEP	A,B	No	-	Yes[4]	7/89
132-1 - Soil Dissipation	TEP	A	No	-	Yes[5]	7/89
133-3 - Dermal Exposure	TEP	A,B	No	-	No[6]	
133-4 - Inhalation Exposure	TEP	A,B	No	-	No[6]	

1/ TEP = Typical end-use product

2/ The use patterns are coded as follows: A=Terrestrial Food Crop; B=Terrestrial Non-Food Crop

3/ This data has previously been requested in the Comprehensive Data Call In Notice issued April 1987. The time frame for submission of data is the same as required in the April 1987 Notice.

4/ For each end-use, the registrant is required to propose an acceptable reentry interval based either upon data: (a) on dissipation of residues (decline curve), on human exposure to those residues, and on toxicity of the residues; or (b) on determination of that time beyond which there are no detectable dislodgeable or inhalable residues remaining in the worker environment.

5/ Soil dissipation data are required only for uses where workers will be exposed directly to substantial quantities of soil during their work, e.g. for use on potatoes or peanuts if hand harvesting will be performed.

6/ Human-exposure monitoring data may be submitted, if the registrant wishes to use the "allowable exposure method" of determining reentry intervals. The data submitted are limited to foliar and soil dissipation studies, human exposure (and reentry intervals) would be estimated from dislodgeable residues as explained in Subdivision K of the Guidelines. If exposure studies are submitted, both dermal exposure and inhalation exposure must be submitted.

TABLE A
GENERIC DATA REQUIREMENTS FOR METIRAM

Data Requirement	Composition[1]	Use[2] Patterns	Does EPA Have Data to Satisfy This Requirement? (Yes, No or Partially?)	Bibliographic Citation	Must Additional Data be Submitted?	Time Frame for Submission[3]
§158.490 Wildlife and Aquatic Organisms						
AVIAN AND MAMMALIAN TESTING						
71-1 - Avian Oral LD_{50}	TGAI	A,H	No		Yes	1/88 4/
71-2 - Avian Dietary LC_{50}	TGAI	A,H	Yes	108004,108005	No	
71-3 - Wild Mammal Toxicity	TGAI	A,H	No		No	
71-4 - Avian Reproduction	TGAI	A,H	No		No	
71-5 - Simulated and Actual Field Testing						
- Mammals, and Birds	TEP	A,H			No	
AQUATIC ORGANISM TESTING						
72-1 - Freshwater Fish LC_{50}	TGAI	A,H	No		Yes	7/88 4/
72-2 - Acute LC_{50} Freshwater Invertebrates	TGAI	A,H	No		Yes	7/88 4/
72-3 - Acute LC_{50} Estuarine and Marine Organisms	TGAI	A	No		No	

TABLE A
GENERIC DATA REQUIREMENTS FOR METIRAM

Data Requirement	Composition[1]	Use Patterns[2]	Does EPA Have Data to Satisfy This Requirement? (Yes, No or Partially?)	Bibliographic Citation	Must Additional Data be Submitted?	Time Frame for[3] Submission
§158.490 Wildlife and Aquatic Organisms - Continued						
72-4 - Fish Early Life Stage and Invertebrate Life-Cycle	TGAI	A	No		No	
72-5 - Fish Life-Cycle	TGAI	A	No		No	
72-6 - Aquatic Organism Accumulation (Fish)	TGAI	A	No		No	
72-7 - Simulated or Actual Field Testing Aquatic Organisms	TEP	A	No		No	

1/ Composition: TGAI = Technical grade of the active ingredient.

2/ A = Terrestrial, Food Crop, H = Domestic Outdoor.

3/ This data has previously been required in the Comprehensive Data Call In Notice of April 1987. The time frame for submission of data is the same as required in the April 1987 Notice.

4/ Studies have recently been submitted and are currently under review.

TABLE A
GENERIC DATA REQUIREMENTS FOR METIRAM

Data Requirement	Composition[1]	Use[2] Patterns	Does EPA Have Data to Satisfy This Requirement? (Yes, No or Partially?)	Bibliographic Citation	Must Additional Data be Submitted?	Time Frame for Submission
§158.550 Nontarget Insect						
NONTARGET INSECT TESTING - POLLINATORS:						
141-1 - Honey bee acute contact LD_{50}	TGAI	A	Yes	00132710	No	
141-2 - Honey bee - toxicity of residues on foliage	TEP	A	No		No 3/	
141-3 - Honey bee subacute feeding study	[Reserved] 4/					
141-4 - Field testing for pollinators	TEP	A	No		No 5/	
NONTARGET INSECT TESTING - AQUATIC INSECTS:						
142-1 - Acute toxicity to aquatic insects	[Reserved] 6/					
142-2 - Aquatic insect life cycle study	[Reserved] 6/					
142-3 - Simulated or actual field testing for aquatic insects	[Reserved] 6/					

TABLE A
GENERIC DATA REQUIREMENTS FOR METIRAM

Data Requirement	Composition[1]	Use[2] Patterns	Does EPA Have Data to Satisfy This Requirement? (Yes, No or Partially?)	Bibliographic Citation	Must Additional Data be Submitted?	Time Frame for Submission
§158.550 Nontarget Insect						
NONTARGET INSECT TESTING - POLLINATORS:						
141-1 - Honey bee acute contact LD_{50}	TGAI	A	Yes	00132710	No	
141-2 - Honey bee - toxicity of residues on foliage	TEP	A	No		No 3/	
141-3 - Honey bee subacute feeding study	[Reserved] 4/					
141-4 - Field testing for pollinators	TEP	A	No		No 5/	
NONTARGET INSECT TESTING - AQUATIC INSECTS:						
142-1 - Acute toxicity to aquatic insects	[Reserved] 6/					
142-2 - Aquatic insect life cycle study	[Reserved] 6/					
142-3 - Simulated or actual field testing for aquatic insects	[Reserved] 6/					

TABLE A
GENERIC DATA REQUIREMENTS FOR METIRAM

Data Requirement	Composition[1]	Use[2] Patterns	Does EPA Have Data to Satisfy This Requirement? (Yes, No or Partially?)	Bibliographic Citation	Must Additional Data be Submitted?	Time Frame for Submission
§158.550 Nontarget Insect						
143-1 thru 143-3 - NONTARGET INSECT TESTING - PREDATORS AND PARASITES [Reserved]	6/					

1/ Composition: TGAI = Technical grade of the active ingredient; TEP = Typical end-use product.

2/ Use Patterns are coded as follows: A=Terrestrial, Food Crop

3/ As data from acute contact test indicate low toxicity, data on residual toxicity are not required.

4/ Requirement reserved pending development of test methodology.

5/ Requirement applied on a case-by-case basis. Data reviewed to date do not indicate the need for a field study; if a need arises, registrants will be informed.

6/ Reserved pending Agency decision as to whether the data requirement should be established.

TABLE B

PRODUCT SPECIFIC DATA REQUIREMENTS FOR MANUFACTURING-USE PRODUCTS; METIRAM

Data Requirement	Composition 1/	Does EPA Have Data?	Bibliographic Citation	Must Additional Data be be Submitted?	Time Frame for Submission
Part 158 Subpart C - Product Chemistry					
Product Identity and Composition:					
61-1 - Product Identity and Disclosure of Ingredients	MP	Yes		No	
61-2 - Description of Beginning Materials and Manufacturing Process	MP	Yes	40507102	No	
61-3 - Discussion of Formation of Impurities	MP	Yes	40507102	No	
Analysis and Certification of Product Ingredients					
62-1 - Preliminary Analysis of Product Samples	MP	Partially	40507102	Yes 2/11/	12 Months
62-2 - Certification of Ingredient Limits	MP	Partially		Yes 3/	12 Months
62-3 - Analytical Methods to Verify Certified Limits	MP	Partially	40507102	Yes 4/	12 Months
Physical and Chemical Characteristics					
63-2 - Color	MP	Yes	00149526	No	
63-3 - Physical State	MP	Yes	00149526	No	

TABLE B

PRODUCT SPECIFIC DATA REQUIREMENTS FOR MANUFACTURING-USE PRODUCTS; METIRAM

Data Requirement	Composition[1]	Does EPA Have Data?	Bibliographic Citation	Must Additional Data be be Submitted?	Time Frame for Submission
Part 158 Subpart C - Product Chemistry (Continued)					
Physical and Chemical Characteristics (Continued)					
63-4 - Odor	MP	Yes	00149526	No	
63-7 - Density, Bulk Density, or Specific Gravity	MP	Yes	00149526	No	
63-12 - pH	MP	Yes	40507102	No	
63-14 - Oxidizing or Reducing Action	MP	No	N/A	Yes[5][6]	6 Months
63-15 - Flammability	MP	No	N/A	Yes[5][7]	6 Months
63-16 - Explodability	MP	No	N/A	Yes[5][8]	6 Months
63-17 - Storage Stability	MP	No	N/A	Yes[5]	15 Months
63-18 - Viscosity	MP	N/A	N/A	No[9]	
63-19 - Miscibility	MP	N/A	N/A	No[10]	
63-20 - Corrosion Charasteristics	MP	No	N/A	Yes[5]	15 Months
Other Requirements:					
64-1 - Submittal of samples	N/A	N/A	N/A	No	

TABLE B

PRODUCT SPECIFIC DATA REQUIREMENTS FOR MANUFACTURING-USE PRODUCTS; METIRAM

Part 158
Subpart C - Product Chemistry (Continued)

1/ Composition: MP = Manufacturing-Use Product.

2/ Five or more representative samples of the 80% FIs (EPA Reg. Nos. 279-2514 and 7969-71) must be analyzed for the amount of active ingredient and each impurity for which certified limits are required. The active ingredient in these samples must be analyzed for metiram *per se* using a method capable of differentiating metiram from interfering CS_2-liberating impurities. If the CS_2-liberation and metiram specific methods yield different results, the CS_2-liberating impurities must be quantified. Complete validation data (accuracy and precision) must be submitted for each analytical method used.

3/ Upper and lower limits for the active ingredient based on the analyses of metiram *per se* using a method capable of differentiating metiram from interfering CS_2-liberating impurities for the 80% FIs (EPA Reg. Nos. 279-2514 and 7969-71) must be submitted. Also, upper limits for each impurity associated with the active ingredient present at ≥0.1% (w/w) and each "toxicologically significant" impurity associated with the active ingredient present at <0.1% (w/w) must provided and certified. Limits for impurities not associated with the active ingredient need be provided only if the are considered to be of toxicological concern, regardless of the concentration at which they are present. An explanation of how each certified limit was established must be provided (e.g., sample analysis using validated analytical procedures, quantitative estimate based on amounts of ingredients used, ets.).

4/ Analytical methods must be provided for the 80% FIs to determine the active ingredient and each impurity for which a certified limit is required. The analytical method for the active ingredient must be able to differentiate metiram *per se* from interfering CS_2-liberating impurities. For CS_2-liberating impurities, HPLC methodology may be most appropriate for achieving the required specificity. All methods must be accompanied by validation studies indicating accuracy and precision. These methods must be suitable for *enforcement* of certified limits.

5/ As required in 40 CFR 158.120 and more fully described in the Pesticide Assessment Guidelines, Subdivision D, data on oxidizing or reducing action, flammability, explodability, storage stability, and corrosion characteristics must be submitted for the 80% FIs (EPA Reg. Nos. 279-2514 and 7969-71).

6/ Data required if the product contains an oxidizing or reducing agent.

7/ Data required if the product contains combustible liquids.

8/ Data required if the product is potentially explosive.

9/ No data are required because the 80% FI is not a liquid at room temperature.

10/ Data are not required because the 80% FI is not a liquid at room temperature nor is it to be diluted with petroleum solvents.

11/ All nitrosamines must be identified and quantified in six samples; two samples of each must be analyzed shortly after production, 3 months after production and 6 months after production. A method sensitive to 1 ppm of N-nitroso contaminants must be used.

APPENDIX II

SUMMARY-1

LABEL CONTENTS

40 CFR 156.10 requires that certain specific labeling statements appear at certain locations on the label. This is referred to as format labeling. Specific label items listed below are keyed to the table at the end of this Appendix.

Item 1. PRODUCT NAME - The name, brand or trademark is required to be located on the front panel, preferably centered in the upper part of the panel. The name of a product will not be accepted if it is false or misleading.

Item 2. COMPANY NAME AND ADDRESS - The name and address of the registrant or distributor is required on the label. The name and address should preferably be located at the bottom of the front panel or at the end of the label text.

Item 3. NET CONTENTS - A net contents statement is required on all labels or on the container of the pesticide. The preferred location is the bottom of the front panel immediately above the company name and address, or at the end of the label text. The net contents must be expressed in the largest suitable unit, e.g., "1 pound 10 ounces" rather than "26 ounces." In addition to English units, net contents may be expressed in metric units. [40 CFR 156.10(d)]

Item 4. EPA REGISTRATION NUMBER - The registration number assigned to the pesticide product must appear on the label, preceded by the phrase "EPA Registration No.," or "EPA Reg. No." The registration number must be set in type of a size and style similar to other print on that part of the label on which it appears and must run parallel to it. The registration number and the required identifying phrase must not appear in such a manner as to suggest or imply recommendation or endorsement of the product by the Agency. [40 CFR 156.10(e)]

Item 5. EPA ESTABLISHMENT NUMBER - The EPA establishment number, preceded by the phrase "EPA Est." is the final establishment at which the product was produced, and may appear in any suitable location on the label or immediate container. It must also appear on the wrapper or outside container of the package if the EPA establishment number on the immediate container cannot be clearly read through such wrapper or container. [40 CFR 156.10(f)]

Item 6A. INGREDIENTS STATEMENT - An ingredients statement is required on the front panel. The ingredients statement must contain the name and percentage by weight of each active ingredient and the total percentage by weight of all inert ingredients. The preferred location is immediately below the product name. The ingredients statement must run parallel with, and be clearly distinguished from, other text on the panel. It must not be placed in the body of other text. [40 CFR 156.10(g)]

Item 6B. POUNDS PER GALLON STATEMENT - For liquid agricultural formulations, the pounds per gallon of active ingredient must be indicated on the label.

Item 7. FRONT LABEL PRECAUTIONARY STATEMENTS - Front panel precautionary statements must be grouped together, preferably within a block outline. The table below shows the minimum type size requirements for various size labels.

Size of Label on Front Panel in Square Inches	Signal Word Minimum Type Size All Capitals	"Keep Out of Reach of Children" Minimum Type Size
5 and under	6 point	6 point
above 5 to 10	10 point	6 point
above 10 to 15	12 point	8 point
above 15 to 30	14 point	10 point
over 30	18 point	12 point

Item 7A. CHILD HAZARD WARNING STATEMENT - The statement "Keep Out of Reach of Children" must be located on the front panel above the signal word except where contact with children during distribution or use is unlikely. [40 CFR 156.10(h)(1)(ii)]

Item 7B. SIGNAL WORD - The signal word (DANGER, WARNING, or CAUTION) is required on the front panel immediately below the child hazard warning statement. [40 CFR 156.10(h)(1)(i)]

Item 7C. SKULL & CROSSBONES AND WORD "POISON" - On products assigned a toxicity Category I on the basis of oral, dermal, or inhalation toxicity, the word "Poison" shall appear on the label in red on a background of distinctly contrasting color and the skull and crossbones shall appear in immediate proximity to the word POISON. [40 CFR 156.10(h)(1)(i)]

Item 7D. STATEMENT OF PRACTICAL TREATMENT - A statement of practical treatment (first aid or other) shall appear on the label of pesticide products in toxicity Categories I, II, and III. [40 CFR 156.10(h)(1)(iii)]

Item 7E. REFERRAL STATEMENT - The statement "See Side (or Back) Panel for Additional Precautionary Statements" is required on the front panel for all products, unless all required precautionary statements appear on the front panel. [40 CFR 156.10(h)(1)(iii)]

Item 8. SIDE/BACK PANEL PRECAUTIONARY LABELING - The precautionary statements listed below must appear together on the label under the heading "PRECAUTIONARY STATEMENTS." The preferred location is at the top of the side or back panel preceding the directions for use, and it is preferred that these statements be surrounded by a block outline. Each of the three hazard warning statements must be headed by the appropriate hazard title. [40 CFR 156.10(h)(2)].

Item 8A. HAZARD TO HUMANS AND DOMESTIC ANIMALS - Where a hazard exists to humans or domestic animals, precautionary statements are required indicating the particular hazard, the route(s) of exposure and the precautions to be taken to avoid accident, injury or damage. [40 CFR 156.10(h)(2)(i)]

Item 8B. ENVIRONMENTAL HAZARD - Where a hazard exists to non-target organisms excluding humans and domestic animals, precautionary statements are required stating the nature of the hazard and the appropriate precautions to avoid potential accident, injury, or damage. [40 CFR 156.10(h)(2)(ii)]

Item 8C. PHYSICAL OR CHEMICAL HAZARD - FLAMMABILITY Precautionary statements relating to flammability of a product are required to appear on the label if it meets the criteria in the PHYS/CHEM Labeling Appendix. The requirement is based on the results of the flashpoint determinations and flame extension tests required to be submitted for all products. These statements are to be located in the side/back panel precautionary statements section, preceded by the heading "Physical/Chemical Hazards." Note that no signal word is used in conjunction with the flammability statements.

Item 9A. RESTRICTED USE CLASSIFICATION - FIFRA sec. 3(d) requires that all pesticide formulations/uses be classified for either general or restricted use. Products classified for restricted use may be limited to use by certified applicators or persons under their direct supervision (or may be subject to other restrictions that may be imposed by regulation).

In the Registration Standard, the Agency has (1) indicated certain formulations/uses are to be restricted (Section IV indicates why the product has been classified for restricted use); or (2) reserved any classification decision until appropriate data are submitted.

The Regulatory Position and Rationale states whether products containing this active ingredient are classified for restricted use. If they are restricted the draft label(s) submitted to the Agency as part of your application must reflect this determination (see below).

If you do not believe that your product should be classified for restricted use, you must submit any information and rationale with your application for reregistration. During the Agency's review of your application, your proposed classification determination will be evaluated in accordance with the provisions of 40 CFR Part 152, Subpart I. You will be notified of the Agency's classification decision.

Classification Labeling Requirements

If your product has been classified for restricted use, the following label requirements apply:

1. All uses restricted.

a. The statement "Restricted Use Pesticide" must appear at the top of the front panel of the label. The statement must be set in type of the same minimum size as required for human hazard signal word (see table in 40 CFR 162.10(h)(1)(iv)

b. Directly below this statement on the front panel, a summary statement of the terms of restriction must appear (including the reasons for restriction if specified in Section I). If use is restricted to certified applicators, the following statement is required: "For retail sale to and use only by Certified Applicators or persons under their direct supervision and only for those uses covered by the Certified Applicator's Certification."

2. Some but not all uses restricted. If the Regulatory Position and Rationale states that some uses are classified for restricted use, and some are unclassified, several courses of action are available:

a. You may label the product for Restricted use. If you do so, you may include on the label uses that are unrestricted, but you may not distinguish them on the label as being unrestricted.

b. You may delete all restricted uses from your label and submit draft labeling bearing only unrestricted uses.

c. You may "split" your registration, i.e., register two separate products with identical formulations, one bearing only unrestricted uses, and the other bearing restricted uses. To do so, submit two applications for reregistration, each containing all forms and necessary labels. Both applications should be submitted simultaneously. Note that the products will be assigned separate registration numbers.

Item 9B. MISUSE STATEMENT - All products must bear the misuse statement, "It is a violation of Federal law to use this product in a manner inconsistent with its labeling." This statement appears at the beginning of the directions for use, directly beneath the heading of that section.

Item 10A. REENTRY STATEMENT - If a reentry interval has been established by the Agency, it must be included on the label. Additional worker protection statements may be required in accordance with PR Notice 83-2, March 29, 1983.

Item 10B. STORAGE AND DISPOSAL BLOCK - All labels are required to bear storage and disposal statements. These statements are developed for specific containers, sizes, and chemical content. These instructions must be grouped and appear under the heading "Storage and Disposal" in the directions for use. This heading must be set in the same type sizes as required for the child hazard warning. Refer to Appendix II, STOR, PEST/DIS, and CONT/DIS to determine the storage and disposal instructions appropriate for your products.

Item 10C. DIRECTIONS FOR USE - Directions for use must be stated in terms which can be easily read and understood by the average person likely to use or to supervise the use of the pesticide. When followed, directions must be adequate to protect the public from fraud and from personal injury and to prevent unreasonable adverse effects on the environment. [40 CFR 156.10]

COLLATERAL LABELING

Bulletins, leaflets, circulars, brochures, data sheets, flyers, or other written or graphic printed matter which is referred to on the label or which is to accompany the product are termed collateral labeling. Such labeling may not bear claims or representations that differ in substance from those accepted in connection with registration of the product. It should be made part of the response to this notice and submitted for review.

SUMMARY-6

LABELING REQUIREMENTS OF THE FIFRA, AS AMENDED

ITEM	LABEL ELEMENT	APPLICABILITY OF REQUIREMENT	PLACEMENT ON LABEL		COMMENTS
			REQUIRED	PREFERRED	
1	Product name	All products	Front panel	Center front panel	
2	Company name and address	All products	None	Bottom front panel or end of label text	If registrant is not the producer, must be qualified by "Packed for . . .," "Distributed by. . .," etc.
3	Net contents	All products	None	Bottom front panel or end of label text	May be in metric units in addition to U.S. units
4	EPA Reg. No.	All products	None	Front panel	Must be in similar type size and run parallel to other type.
5	EPA Est. No.	All products	None	Front panel, immediately before or following Reg. No.	May appear on the container instead of the label.
6A	Ingredients statement	All products	Front panel	Immediately following product name	Text must run parallel with other text on the panel.
6B	Pounds/gallon statement	Liquid products where dosage given as lbs. ai/unit area	Front panel	Directly below the main ingredients statement	
7	Front panel precautionary statements	All products	Front panel		All front panel precautionary statements must be grouped together, preferably blocked.
7A	Keep Out of Reach of Children (Child hazard warning)	All products	Front panel	Above signal word	Note type size requirements.
7B	Signal word	All products	Front panel	Immediately below child hazard warning	Note type size requirements.

ITEM	LABEL ELEMENT	APPLICABILITY OF REQUIREMENT	PLACEMENT ON LABEL		COMMENTS
			REQUIRED	PREFERRED	
7C	Skull & crossbones and word POISON (in red)	All products which are Category I based on oral, dermal, or inhalation toxicity	Front panel	Both in close proximity to signal word	
7D	Statement of Practical Treatment or First Aid	All products in Categories I, II, and III	Category I: Front panel unless referral statement is used. Others: Grouped with side panel precautionary statements.	Front panel for all.	
7E	Referral statement	All products where precautionary labeling appears on other than front panel.	Front panel		
8	Side/back panel precautionary statements	All products	None	Top or side of back panel preceding directions for use	Must be grouped under the headings in 8A, 8B, and 8C; preferably blocked.
8A	Hazards to humans and domestic animals	All products in Categories I, II, and III	None	Same as above	Must be preceded by appropriate signal word.
8B	Environmental hazards	All products	None	Same as above	Environmental hazards include bee caution where applicable.

ITEM	LABEL ELEMENT	APPLICABILITY OF REQUIREMENT	PLACEMENT ON LABEL		COMMENTS
			REQUIRED	PREFERRED	
8C	Physical or chemical hazards	All pressurized products, others with flash points under 150°F	None	Same as above	Refer to Appendix II guide PHYS/CHEM
9A	Restricted block	All restricted products	Top center of front panel	Preferably blocked	Includes a statement of the terms of restriction. The words "RESTRICTED USE PESTICIDE" must be same type size as signal word.
9B	Misuse statement	All products	Immediately following heading of directions for use		Required statement is: "It is a violation of Federal law to use this product in a manner inconsistent with its labeling."
10A	Reentry statement	PR Notice 83-2 or as determined by the Agency	In the directions for use	Immediately after misuse statement	
10B	Storage and disposal block	All products	In the directions for use	Immediately before specific directions for use or at the end of directions for use	Must be set apart and clearly distinguishable from from other directions for use. Refer to Appendix II guides STOR, CONT/DIS, and PEST/DIS for further information and required statements.
10C	Directions for use	All products	None	None	May be in metric as well as U.S. units

PHYSICAL/CHEMICAL HAZARDS

Criteria	Required Label Statement
I. Pressurized Containers	
A. Flashpoint at or below 20°F; or if there is a flashback at any valve opening.	Extremely flammable. Contents under pressure. Keep away from fire, sparks, and heated surfaces. Do not puncture or incinerate container. Exposure to temperatures above 130°F may cause bursting.
B. Flashpoint above 20°F and not over 80°F; or if the flame extension is more than 18 inches long at a distance of 6 inches from the valve opening.	Flammable. Contents under pressure. Keep away from heat, sparks, and flame. Do not puncture or incinerate container. Exposure to temperatures above 130°F may cause bursting.
C. All Other Pressurized Containers	Contents under pressure. Do not use or store near heat or open flame. Do not puncture or incinerate container. Exposure to temperatures above 130°F may cause bursting.
II. Non-Pressurized Containers	
A. Flashpoint at or below 20°F.	Extremely flammable. Keep away from fire, sparks, and heated surfaces.
B. Flashpoint above 20°F and not over 80°F.	Flammable. Keep away from heat and open flame.
C. Flashpoint over 80°F and not over 150°F.	Do not use or store near heat and open flame.
D. Flashpoint above 150°F.	None required.

STOR-1

STORAGE INSTRUCTIONS FOR PESTICIDES

Heading:

All products are required to bear specific label instructions about storage and disposal. Storage and disposal instructions must be grouped together in the directions for use portion of the label under the heading STORAGE AND DISPOSAL. Products intended solely for domestic use need not include the heading "STORAGE AND DISPOSAL."

Storage Instructions:

All product labels are required to have appropriate storage instructions. Specific storage instructions are not prescribed. Each registrant must develop his own storage instructions, considering, when applicable, the following factors:

1. Conditions of storage that might alter the composition or usefulness of the pesticide. Examples could be temperature extremes, excessive moisture or humidity, heat, sunlight, friction, or contaminating substances or media.

2. Physical requirements of storage which might adversely affect the container of the product and its ability to continue to function properly. Requirements might include positioning of the container in storage, storage or damage due to stacking, penetration of moisture, and ability to withstand shock or friction.

3. Specifications for handling the pesticide container, including movement of container within the storage area, proper opening and closing procedures (particularly for opened containers), and measures to minimize exposure while opening or closing container.

4. Instructions on what to do if the container is damaged in any way, or if the pesticide is leaking or has been spilled, and precautions to minimize exposure if damage occurs.

5. General precautions concerning locked storage, storage in original container only, and separation of pesticides during storage to prevent cross-contamination of other pesticides, fertilizer, food, and feed.

6. General storage instructions for household products should emphasize storage in original container and placement in locked storage areas.

CONTAINER DISPOSAL INSTRUCTIONS

The label of each product must bear container disposal instructions appropriate to the type of container.

1. Domestic use products must bear one of the following container disposal statements:

Container Type	Statement
Non-aerosol products (bottles, cans, jars)	Do not reuse container (bottle, can, jar). Rinse thoroughly before discarding in trash.
Non-aerosol products (bags)	Do not reuse bag. Discard bag in trash.
Aerosol products	Replace cap and discard containers in trash. Do not incinerate or puncture.

2. All other products must bear container disposal instructions, based on container type, listed below:

Container Type	Statement
Metal containers (non-aerosol)	Triple rinse (or equivalent). Then offer for recycling or reconditioning, or puncture and dispose of in a sanitary landfill, or by other procedures approved by state and local authorities.
Plastic containers	Triple rinse (or equivalent). Then offer for recycling or reconditioning, or puncture and dispose of in a sanitary landfill, or incineration, or, if allowed by state and local authorities, by burning. If burned, stay out of smoke.
Glass containers	Triple rinse (or equivalent). Then dispose of in a sanitary landfill or by other approved state and local procedures.
Fiber drums with liners	Completely empty liner by shaking and tapping sides and bottom to loosen clinging particles. Empty residue into application equipment. Then dispose of liner in a sanitary landfill or by incineration if allowed by state and local authorities. If drum is contaminated and cannot be reused[1], dispose of in the same manner.
Paper and plastic bags	Completely empty bag into application equipment. Then dispose of empty bag in a sanitary landfill or by incineration, or, if allowed by State and local authorities, by burning. If burned, stay out of smoke.
Compressed gas cylinders	Return empty cylinder for reuse (or similar wording)

1/ Manufacturer may replace this phrase with one indicating whether and how fiber drum may be reused.

PESTICIDE DISPOSAL INSTRUCTIONS

The label of all products, except those intended solely for domestic use, must bear explicit instructions about pesticide disposal. The statements listed below contain the exact wording that must appear on the label of these products:

1. The labels of all products, except domestic use, must contain the statement, "Do not contaminate water, food, or feed by storage or disposal."

2. Except those products intended solely for domestic use, the labels of all products that contain active ingredients that are Acute Hazardous Wastes or are assigned to Toxicity Category I on the basis of oral or dermal toxicity, or Toxicity Category I or II on the basis of acute inhalation toxicity must bear the following pesticide disposal statement:

> "Pesticide wastes are acutely hazardous. Improper disposal of excess pesticide, spray mixture, or rinsate is a violation of Federal Law. If these wastes cannot be disposed of by use according to label instructions, contact your State Pesticide or Environmental Control Agency, or the Hazardous Waste representative at the nearest EPA Regional Office for guidance."

3. The labels of all products, except those intended for domestic use, containing active or inert ingredients that are Toxic Hazardous Wastes or meet any of the criteria in 40 CFR 261, Subpart C for a hazardous waste must bear the following pesticide disposal statement:

> "Pesticide wastes are toxic. Improper disposal of excess pesticide, spray mixture, or rinsate is a violation of Federal Law. If these wastes cannot be disposed of by use according to label instructions, contact your State Pesticide or Environmental Control Agency, or the Hazardous Waste representative at the nearest EPA Regional Office for guidance."

4. Labels for all other products, except those intended for domestic use, must bear the following pesticide disposal statement:

> "Wastes resulting from the use of this product may be disposed of on site or at an approved waste disposal facility."

5. Products intended for domestic use only must bear the following disposal statement: "Securely wrap original container in several layers of newspaper and discard in trash."

Chapter 1--Environmental Protection Agency

§156.10 Labeling Requirements
previously cited as §162.10

(a) General--(1) Contents of the label. Every pesticide product shall bear a label containing the information specified by the Act and the regulations in this Part. The contents of a label must show clearly and prominently the following:

(i) The name, brand, or trademark under which the product is sold as prescribed in paragraph (b) of this section;

(ii) The name and address of the producer, registrant, or person for whom produced as prescribed in paragraph (c) of this section;

(iii) The net contents as prescribed in paragraph (d) of this section;

(iv) The product registration number as prescribed in paragraph (e) of this section;

(v) The producing establishment number as prescribed in paragraph (f) of this section;

(vi) An ingredient statement as prescribed in paragraph (g) of this section;

(vii) Warning or precautionary statements as prescribed in paragraph (h) of this section;

(viii) The directions for use as prescribed in paragraph (i) of this section; and

(ix) The use classification(s) as prescribed in paragraph (j) of this section.

(2) Prominence and legibility. (i) All words, statements, graphic representations, designs or other information required on the labeling by the Act or the regulations in this part must be clearly legible to a person with normal vision, and must be placed with such conspicuousness (as compared with other words, statements, designs, or graphic matter on the labeling) and expressed in such terms as to render it likely to be read and understood by the ordinary individual under customary conditions of purchase and use.

(ii) All required label text must:

(A) Be set in 6-point or larger type;

(B) Appear on a clear contrasting background; and

(C) Not be obscured or crowded.

(3) Language to be used. All required label or labeling text shall appear in the English language. However, the Agency may require or the applicant may propose additional text in other languages as is considered necessary to protect the public. When additional text in another language is necessary, all labeling requirements will be applied equally to both the English and other-language versions of the labeling.

(4) Placement of Label--(i) General. The label shall appear on or be securely attached to the immediate container of the

pesticide product. For purposes of this Section, and the misbranding provisions of the Act, "securely attached" shall mean that a label can reasonably be expected to remain affixed during the foreseeable conditions and period of use. If the immediate container is enclosed within a wrapper or outside container through which the label cannot be clearly read, the label must also be securely attached to such outside wrapper or container, if it is a part of the package as customarily distributed or sold.

(ii) Tank cars and other bulk containers--(A) Transportation. While a pesticide product is in transit, the appropriate provisions of 49 CFR Parts 170-189, concerning the transportation of hazardous materials, and specifically those provisions concerning the labeling, marking and placarding of hazardous materials and the vehicles carrying them, define the basic Federal requirements. In addition, when any registered pesticide product is transported in a tank car, tank truck or other mobile or portable bulk container, a copy of the accepted label must be attached to the shipping papers, and left with the consignee at the time of delivery.

(B) Storage. When pesticide products are stored in bulk containers, whether mobile or stationary, which remain in the custody of the user, a copy of the label of labeling, including all appropriate directions for use, shall be securely attached to the container in the immediate vicinity of the discharge control valve.

(5) False or misleading statements. Pursuant to section 2(q)(1)(A) of the Act, a pesticide or a device declared subject to the Act pursuant to § 162.15, is misbranded if its labeling is false or misleading in any particular including both pesticidal and non-pesticidal claims. Examples of statements or representations in the labeling which constitute misbranding include:

(i) A false or misleading statement concerning the composition of the product;

(ii) A false or misleading statement concerning the effectiveness of the product as a pesticide or device;

(iii) A false or misleading statement about the value of the product for purposes other than as a pesticide or device;

(iv) A false or misleading comparison with other pesticides or devices;

(v) Any statement directly or indirectly implying that the pesticide or device is recommended or endorsed by any agency of the Federal Government;

(vi) The name of a pesticide which contains two or more principal active ingredients if the name suggests one or more but not all such principal active ingredients even though the names of the other ingredients are stated elsewhere in the labeling;

(vii) A true statement used in such a way as to give a false or misleading impression to the purchaser;

(viii) Label disclaimers which negate or detract from labeling statements required under the Act and these regulations;

(ix) Claims as to the safety of the pesticide or its ingredients, including statements such as "safe," "nonpoisonous," "noninjurious," "harmless" or "nontoxic to humans and pets" with or without such a qualifying phrase as "when used as directed"; and

(x) Non-numerical and/or comparative statements on the safety of the product, including but not limited to:

(A) "Contains all natural ingredients";

(B) "Among the least toxic chemicals known"

(C) "Pollution approved"

(6) Final printed labeling. (i) Except as provided in paragraph (a)(6)(ii) of this section, final printed labeling must be submitted and accepted prior to registration. However, final printed labeling need not be submitted until draft label texts have been provisionally accepted by the Agency.

(ii) Clearly legible reproductions or photo reductions will be accepted for unusual labels such as those silk-screened directly onto glass or metal containers or large bag or drum labels. Such reproductions must be of microfilm reproduction quality.

(b) Name, brand, or trademark. (1) The name, brand, or trademark under which the pesticide product is sold shall appear on the front panel of the label.

(2) No name, brand, or trademark may appear on the label which:

(i) Is false or misleading, or

(ii) Has not been approved by the Administrator through registration or supplemental registration as an additional name pursuant to § 162.6(b)(4).

(c) Name and address of producer, registrant, or person for whom produced. An unqualified name and address given on the label shall be considered as the name and address of the producer. If the registrant's name appears on the label and the registrant is not the producer, or if the name of the person for whom the pesticide was produced appears on the label, it must be qualified by appropriate wording such as "Packed for ***," "Distributed by ***," or "Sold by ***" to show that the name is not that of the producer.

(d) Net weight or measure of contents. (1) The net weight or measure of content shall be exclusive of wrappers or other materials and shall be the average content unless explicitly stated as a minimum quantity.

(2) If the pesticide is a liquid, the net content statement shall be in terms of liquid measure at 68°F (20°C) and shall be expressed in conventional American units of fluid ounces, pints, quarts, and gallons.

(3) If the pesticide is solid or semisolid, viscous or pressurized, or is a mixture of liquid and solid, the net content statement shall be in terms of weight expressed as avoirdupois pounds and ounces.

(4) In all cases, net content shall be stated in terms of the largest suitable units, i.e., "1 pound 10 ounces" rather than "26 ounces."

(5) In addition to the required units specified, net content may be expressed in metric units.

(6) Variation above minimum content or around an average is permissible only to the extent that it represents deviation unavoidable in good manufacturing practice. Variation below a stated minimum is not permitted. In no case shall the average content of the packages in a shipment fall below the stated average content.

(e) Product registration number. The registration number assigned to the pesticide product at the time of registration shall appear on the label, preceded by the phrase "EPA Registration No.," or the phrase "EPA Reg. No." The registration number shall be set in type of a size and style similar to other print on that part of the label on which it appears and shall run parallel to it. The registration number and the required identifying phrase shall not appear in such a manner as to suggest or imply recommendation or endorsement of the product by the Agency.

(f) Producing establishments registration number. The producing establishment registration number preceded by the phrase "EPA Est.", of the final establishment at which the product was produced may appear in any suitable location on the label or immediate container. It must appear on the wrapper or outside container of the package if the EPA establishment registration number on the immediate container cannot be clearly read through such wrapper or container.

(g) Ingredient statement--(1) General. The label of each pesticide product must bear a statement which contains the name and percentage by weight of each active ingredient, the total percentage by weight of all inert ingredients; and if the pesticide contains arsenic in any form, a statement of the percentages of total and water-soluble arsenic calculated as elemental arsenic. The active ingredients must be designated by the term "active ingredients" and the inert ingredients by the term "inert ingredients," or the singular forms of these terms when appropriate. Both terms shall be in the same type size, be aligned to the same margin and be equally prominent. The statement "Inert Ingredients, none" is not required for pesticides which contain 100 percent active ingredients. Unless the ingredient statement is a complete analysis of the pesticide, the term "analysis" shall not be used as a heading for the ingredient statement.

(2) Position of ingredient statement. (i) The ingredient statement is normally required on the front panel of the label. If there is an outside container or wrapper through which the ingredient statement cannot be clearly read, the ingredient statement must also appear on such outside container or wrapper. If the size or form of the package makes it impracticable to place the ingredient statement on the front panel of the label, permission may be granted for the ingredient statement to appear elsewhere.

(ii) The text of the ingredient statement must run parallel with other text on the panel on which it appears, and must be clearly distinguishable from and must not be placed in the body of other text.

(3) Names to be used in ingredient statement. The name used for each ingredient shall be the accepted common name, if there is one, followed by the chemical name. The common name may be used alone only if it is well known. If no common name has been established, the chemical name alone shall be used. In no case will the use of a trademark or proprietary name be permitted unless such name has been accepted as a common name by the Administrator under the authority of Section 25(c)(6).

(4) Statements of percentages. The percentages of ingredients shall be stated in terms of weight-to-weight. The sum of percentages of the active and the inert ingredients shall be 100. Percentages shall not be expressed by a range of values such as "22-25%." If the uses of the pesticide product are expressed as weight of active ingredient per unit area, a statement of the weight of active ingredient per unit volume of the pesticide formulation shall also appear in the ingredient statement.

(5) Accuracy of stated percentages. The percentages given shall be as precise as possible reflecting good manufacturing practice. If there may be unavoidable variation between manufacturing batches, the value stated for each active ingredient shall be the lowest percentage which may be present.

(6) Deterioration. Pesticides which change in chemical composition significantly must meet the following labeling requirements:

(i) In cases where it is determined that a pesticide formulation changes chemical composition significantly, the product must bear the following statement in a prominent position on the label: "Not for sale or use after [date]."

(ii) The product must meet all label claims up to the expiration time indicated on the label.

(7) Inert ingredients. The Administrator may require the name of any inert ingredient(s) to be listed in the ingredient statement if he determines that such ingredient(s) may pose a hazard to man or the environment.

(h) Warnings and precautionary statements. Required warnings and precautionary statements concerning the general areas of toxicological hazard including hazard to children, environmental hazard, and physical or chemical hazard fall into two groups; those required on the front panel of the labeling and those which may appear elsewhere. Specific requirements concerning content, placement, type size, and prominence are given below.

(1) Required front panel statements. With the exception of the child hazard warning statement, the text required on the front panel of the label is determined by the Toxicity Category of the pesticide. The category is assigned on the basis of the highest hazard shown by any of the indicators in the table below:

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Hazard indicators	Toxicity categories			
	I	II	III	IV
Oral LD_{50}	Up to and including 50 mg/kg	From 50 thru 500 mg/kg	From 500 thru 5000 mg/kg	Greater than 5000 mg/kg
Inhalation LC_{50}	Up to and including .2 mg/liter	From .2 thru 2 mg/liter	From 2 thru 20 mg/liter	Greater than 20 mg/liter
Dermal LD_{50}	Up to and including 200 mg/kg	From 200 thru 2000	From 2,000 thru 20,000	Greater than 20,000
Eye effects	Corrosive; corneal opacity not reversible within 7 days	Corneal opacity reversible within 7 days; irritation persisting for 7 days	No corneal opacity; irritation reversible within 7 days	No irritation
Skin effects	Corrosive	Severe irritation at 72 hours	Moderate irritation at 72 hours	Mild or slight irritation at 72 hours

(i) Human hazard signal word.--(A) Toxicity Category I. All pesticide products meeting the criteria of Toxicity Category I shall bear on the front panel the signal word "Danger." In addition if the product was assigned to Toxicity Category I on the basis of its oral, inhalation or dermal toxicity (as distinct from skin and eye local effects) the word "Poison" shall appear in red on a background of distinctly contrasting color and the skull and crossbones shall appear in immediate proximity to the word "poison."

(B) Toxicity Category II. All pesticide products meeting the criteria of Toxicity Category II shall bear on the front panel the signal word "Warning."

(C) Toxicity Category III. All pesticide products meeting the criteria of Toxicity Category III shall bear on the front panel the signal word "Caution."

(D) Toxicity Category IV. All pesticide products meeting the criteria of Toxicity Category IV shall bear on the front panel the signal word "Caution."

(E) Use of signal words. Use of any signal word(s) associated with a higher Toxicity Category is not permitted except when the Agency determines that such labeling is necessary to prevent unreasonable adverse effects on man or the environment. In no case shall more than one human hazard signal word appear on the front panel of a label.

(ii) Child hazard warning. Every pesticide product label shall bear on the front panel the statement "keep out of reach of children." Only in cases where the likelihood of contact with children during distribution, marketing, storage or use is demonstrated by the applicant to be extremely remote, or if the nature of the pesticide is such that it is approved for use on infants or small children, may the Administrator waive this requirement.

(iii) Statement of practical treatment--(A) Toxicity Category I. A statement of practical treatment (first aid or other) shall appear on the front panel of the label of all pesticides falling into Toxicity Category I on the basis of oral, inhalation or dermal toxicity. The Agency may, however, permit reasonable variations in the placement of the statement of practical treatment is some reference such as "See statement of practical treatment on back panel" appears on the front panel near the word "Poison" and the skull and crossbones.

(B) Other toxicity categories. The statement of practical treatment is not required on the front panel except as described in paragraph (h)(1)(iii)(A) of this section. The applicant may, however, include such a front panel statement at his option. Statements of practical treatment are, however, required elsewhere on the label in accord with paragraph (h)(2) of this section if they do not appear on the front panel.

(iv) Placement and prominence. All the required front panel warning statements shall be grouped together on the label, and shall appear with sufficient prominence relative to other front panel text and graphic material to make them unlikely to be overlooked under customary conditions of purchase and use. The following table shows the minimum type size requirements for the front panel warning statements on various sizes of labels:

Size of label front panel in square inches	Points	
	Required signal word, all capitals	"Keep out of reach of Children"
5 and under	6	6
Above 5 to 10	10	6
Above 10 to 15	12	8
Above 15 to 30	14	10
Over 30	18	12

(2) Other required warnings and precautionary statements. The warnings and precautionary statements as required below shall appear together on the label under the general heading "Precautionary Statements" and under appropriate subheadings of "Hazard to Humans and Domestic Animals," "Environmental Hazard" and "Physical or Chemical Hazard."

(i) Hazard to humans and domestic animals. (A) Where a hazard exists to humans or domestic animals, precautionary statements are required indicating the particular hazard, the route(s) of exposure and the precautions to be taken to avoid accident, injury or damage. The precautionary paragraph shall be immediately preceded by the appropriate hazard signal word.

(B) The following table depicts typical precautionary statements. These statements must be modified or expanded to reflect specific hazards.

Toxicity category	Precautionary statements by toxicity category	
	Oral, inhalation, or dermal toxicity	Skin and eye local effects
I . . .	Fatal (poisonous) if swallowed [inhaled or absorbed through skin]. Do not breathe vapor [dust] or spray mist]. Do not get in eyes, on skin, or on clothing [Front panel statement of practical treatment required.].	Corrosive, causes eye and skin damage [or skin irritation]. Do not get in eyes, on skin, or on clothing. Wear goggles or face shield and rubber gloves when handling. Harmful or fatal if swallowed. [Appropriate first aid statement required.]
II . . .	May be fatal if swallowed [inhaled or absorbed through the skin]. Do not breathe vapors [dust or spray mist]. Do not get in eyes, on skin, or on clothing. [Appropriate first aid statements required.].	Causes eye [and skin] irritation. Do not get in eyes, on skin, or on clothing. Harmful if swallowed. [Appropriate first aid statement required.].
III . . .	Harmful if swallowed [inhaled or absorbed through the skin]. Avoid breathing vapors [dust or spray mist]. Avoid contact with skin [eyes or clothing]. [Appropriate first aid statement required.].	Avoid contact with skin, eyes or clothing. In case of contact immediately flush eyes or skin with plenty of water. Get medical attention if irritation persists.
IV . . .	[No precautionary statements required.].	[No precautionary statements required.].

(ii) Environmental hazards. Where a hazard exists to non-target organisms excluding humans and domestic animals, precautionary statements are required stating the nature of the hazard and the appropriate precautions to avoid potential accident, injury or damage. Examples of the hazard statements and the circumstances under which they are required follow:

(A) If a pesticide intended for outdoor use contains an active ingredient with a mammalian acute oral LD_{50} of 100 or less, the statement "This Pesticide is Toxic to Wildlife" is required.

(B) If a pesticide intended for outdoor use contains an active ingredient with a fish acute LC_{50} of 1 ppm or less, the statement "This Pesticide is Toxic to Fish" is required.

(C) If a pesticide intended for outdoor use contains an active ingredient with an avian acute oral LD_{50} of 100 mg/kg or less, or a subacute dietary LC_{50} of 500 ppm or less, the statement "This Pesticide is Toxic to Wildlife" is required.

(D) If either accident history or field studies demonstrate that use of the pesticide may result in fatality to birds, fish or mammals, the statement "This pesticide is extremely toxic to wildlife (fish)" is required.

(E) For uses involving foliar application to agricultural crops, forests, or shade trees, or for mosquito abatement treatments, pesticides toxic to pollinating insects must bear appropriate label cautions.

(F) For all outdoor uses other than aquatic applications the label must bear the caution "Keep out of lakes, ponds or streams. Do not contaminate water by cleaning of equipment or disposal of wastes."

(iii) Physical or chemical hazards. Warning statements on the flammability or explosive characteristics of the pesticide are required as follows:

Flash point	Required text
(A) PRESSURIZED CONTAINERS	
Flash point at or below 20°F; if there is a flashback at any valve opening.	Extremely flammable. Contents under pressure. Keep away from fire, sparks, and heated surfaces. Do not puncture or incinerate container. Exposure to temperatures above 130°F may cause bursting.
Flash point above 20°F and not over 80°F or if the flame extension is more than 18 in. long at a distance of 6 in. from the flame.	Flammable. Contents under pressure. Keep away from heat, sparks, and open flame. Do not puncture or incinerate container. Exposure to temperatures above 130°F may cause bursting.
All other pressurized containers	Contents under pressure. Do not use or store near heat or open flame. Do not puncture or incinerate container. Exposure to temperatures above 130°F may cause bursting.
(B) NONPRESSURIZED CONTAINERS	
At or below 20°F	Extremely flammable. Keep away from fire, sparks, and heated surfaces.
Above 20°F and not over 80°F	Flammable. Keep away from heat and open flame.
Above 80°F and not over 150°F	Do not use or store near heat or open flame.

(i) *Directions for Use*--(1) *General requirements*--(i) *Adequacy and clarity of directions*. Directions for use must be stated in terms which can be easily read and understood by the average person likely to use or to supervise the use of the pesticide. When followed, directions must be adequate to protect the public from fraud and from personal injury and to prevent unreasonable adverse effects on the environment.

(ii) *Placement of directions for use*. Directions may appear on any portion of the label provided that they are conspicuous enough to be easily read by the user of the pesticide product. Directions for use may appear on printed or graphic matter which accompanies the pesticide provided that:

(A) If required by the Agency, such printed or graphic matter is securely attached to each package of the pesticide, or placed within the outside wrapper or bag;

(B) The label bears a reference to the directions for use in accompanying leaflets or circulars, such as "See directions in the enclosed circular." and

(C) The Administrator determines that it is not necessary for such directions to appear on the label.

(iii) *Exceptions to requirement for direction for use*--(A) Detailed directions for use may be omitted from labeling of pesticides which are intended for use only by manufacturers of products other than pesticide products in their regular manufacturing processes, provided that:

(*1*) The label clearly shows that the product is intended for use only in manufacturing processes and specifies the type(s) of products involved.

(*2*) Adequate information such as technical data sheets or bulletins, is available to the trade specifying the type of product involved and its proper use in manufacturing processes;

(*3*) The product will not come into the hands of the general public except after incorporation into finished products; and

(*4*) The Administrator determines that such directions are not necessary to prevent unreasonable adverse effects on man or the environment.

(B) Detailed directions for use may be omitted from the labeling of pesticide products for which sale is limited to physicians, veterinarians, or druggists, provided that:

(*1*) The label clearly states that the product is for use only by physicians or veterinarians;

(*2*) The Administrator determines that such directions are not necessary to prevent unreasonable adverse effects on man or the environment; and

(*3*) The product is also a drug and regulated under the provisions of the Federal Food, Drug and Cosmetic Act.

(C) Detailed directions for use may be omitted from the labeling of pesticide products which are intended for use only by formulators in preparing pesticides for sale to the public, provided that:

(*1*) There is information readily available to the formulators on the composition, toxicity, methods of use, applicable restrictions or limitations, and effectiveness of the product for pesticide purposes;

(2) The label clearly states that the product is intended for use only in manufacturing, formulating, mixing, or repacking for use as a pesticide and specifies the type(s) of pesticide products involved;

(3) The product as finally manufactured, formulated, mixed, or repackaged is registered; and

(4) The Administrator determines that such directions are not necessary to prevent unreasonable adverse effects on man or the environment.

(2) Contents of Directions for Use. The directions for use shall include the following, under the headings "Directions for Use":

(i) The statement of use classification as prescribed in 162.10(j) immediately under the heading "Directions for Use."

(ii) Immediately below the statement of use classification, the statement "It is a violation of Federal law to use this product in a manner inconsistent with its labeling."

(iii) The site(s) of application, as for example the crops, animals, areas, or objects to be treated.

(iv) The target pest(s) associated with each site.

(v) The dosage rate associated with each site and pest.

(vi) The method of application, including instructions for dilution, if required, and type(s) of application apparatus or equipment requried.

(vii) The frequency and timing of applications necessary to obtain effective results without causing unreasonable adverse effects on the environment.

(viii) Specific limitations on reentry to areas where the pesticide has been applied, meeting the requirements concerning reentry provided by 40 CFR Part 170.

(ix) Specific directions concerning the storage and disposal of the pesticide and its container, meeting the requirements of 40 CFR Part 165. These instructions shall be grouped and appear under the heading "Storage and Disposal." This heading must be set in type of the same minimum sizes as required for the child hazard warning (See Table in § 162.10(h)(1)(iv).)

(x) Any limitations or restrictions on use required to prevent unreasonable adverse effects, such as:

(A) Required intervals between application and harvest of food or feed crops.

(B) Rotational crop restrictions.

(C) Warnings as required against use on certain crops, animals, objects, or in or adjacent to certain areas.

(D) [Reserved]

(E) For restricted use pesticides, a statement that the pesticide may be applied under the direct supervision of a certified applicator who is not physically present at the site of application but nonetheless available to the person applying the pesticide, unless the Agency has determined that the pesticide may only be applied under the direct supervision of a certified applicator who is physically present.

(F) Other pertinent information which the Administrator determines to be necessary for the protection of man and the environment.

(j) Statement of Use Classification. By October 22, 1976, all pesticide products must bear on their labels a statement of use classification as described in paragraphs (j)(1) and (2) of this section. Any pesticide product for which some uses are classified for general use and others for restricted use shall be separately labeled according to the labeling standards set forth in this subsection, and shall be marketed as separate products with different registration numbers, one bearing directions only for general use(s) and the other bearing directions for restricted use(s) except that, if a product has both restricted use(s) and general use(s), both of these uses may appear on a product labeled for restricted use. Such products shall be subject to the provisions of § 162.10(j)(2).

(1) General Use Classification. Pesticide products bearing directions for use(s) classified general shall be labeled with the exact words "General Classification" immediately below the heading "Directions for Use." And reference to the general classification that suggests or implies that the general utility of the pesticide extends beyond those purposes and uses contained in the Directions for Use will be considered a false or misleading statement under the statutory definitions of misbranding.

(2) Restricted Use Classification. Pesticide products bearing direction for use(s) classified restricted shall bear statements of restricted use classification on the front panel as described below:

(i) Front panel statement of restricted use classification.
(A) At the top of the front panel of the label, set in type of the same minimum sizes as required for human hazard signal words (see table in § 162.10(h)(1)(iv)), and appearing with sufficient prominence relative to other text and graphic material on the front panel to make it unlikely to be overlooked under customary conditions of purchase and use, the statement "Restricted Use Pesticide" shall appear.

(B) Directly below this statement on the front panel, a summary statement of the terms of restriction imposed as a precondition to registration shall appear. If use is restricted to certified applicators, the following statement is required: "For retail sale to and use only by Certified Applicators or persons under their direct supervision and only for those uses covered by the Certified Applicator's certification." If, however, other regulatory restrictions are imposed, the Administrator will define the appropriate wording for the terms of restriction by regulation.

(k) Advertising. [Reserved]

[40 FR 28268, July 3, 1975; 40 FR 32329, Aug. 1, 1975; 40 FR 38571, Aug. 21, 1975, as amended at 43 FR 5786, Feb. 9, 1978]

APPENDIX III

GUIDE TO USE OF THIS BIBLIOGRAPHY

1. CONTENT OF BIBLIOGRAPHY. This bibliography contains citations of all studies considered relevant by EPA in arriving at the positions and conclusions stated elsewhere in the Standard. Primary sources for studies in this bibliography have been the body of data submitted to EPA and its predecessor agencies in support of past regulatory decisions. Selections from other sources including the published literature, in those instances where they have been considered, will be included.

2. UNITS OF ENTRY. The unit of entry in this bibliography is called a "study." In the case of published materials, this corresponds closely to an article. In the case of unpublished materials submitted to the Agency, the Agency has sought to identify documents at a level parallel to the published article from within the typically larger volumes in which they were submitted. The resulting "studies" generally have a distinct title (or at least a single subject), can stand alone for purposes of review, and can be described with a conventional bibliographic citation. The Agency has attempted also to unite basic documents and commentaries upon them, treating them as a single study.

3. IDENTIFICATION OF ENTRIES. The entries in this bibliography are sorted numerically by "Master Record Identifier," or MRID, number. This number is unique to the citation, and should be used at any time specific reference is required. It is not related to the six-digit "Accession Number" which has been used to identify volumes of submitted studies; see paragraph 4(d)(4) below for a further explanation. In a few cases, entries added to the bibliography late in the review may be preceded by a nine-character temporary identifier. These entries are listed after all MRID entries. This temporary identifier number is also to be used whenever specific reference is needed.

4. FORM OF ENTRY. In addition to the Master Record Identifier (MRID), each entry consists of a citation containing standard elements followed, in the case of material submitted to EPA, by a description of the earliest known submission. Bibliographic conventions used reflect the standards of the American National Standards Institute (ANSI), expanded to provide for certain special needs.

a. Author. Whenever the Agency could confidently identify one, the Agency has chosen to show a personal author. When no individual was identified, the Agency has shown an identifiable laboratory or testing facility as author. As a last resort, the Agency has shown the first submitter as author.

b. Document Date. When the date appears as four digits with no question marks, the Agency took it directly from the document. When a four-digit date is followed by a question mark, the bibliographer deduced the date from evidence in the document. When the date appears as (19??), the Agency was unable to determine or estimate the date of the document.

c. Title. In some cases, it has been necessary for Agency bibliographers to create or enhance a document title. Any such editorial insertions are contained between square brackets.

d. Trailing Parentheses. For studies submitted to the Agency in the past, the trailing parentheses include (in addition to any self-explanatory text) the following elements describing the earliest known submission:

    (1) Submission Date. The date of the earliest known submission appears immediately following the word "received."

    (2) Administrative Number. The next element, immediately following the word "under," is the registration number, experimental use permit number, petition number, or other administrative number associated with the earliest known submission.

    (3) Submitter. The third element is the submitter, following the phrase "submitted by." When authorship is defaulted to the submitter, this element is omitted.

    (4) Volume Identification (Accession Numbers). The final element in the trailing parentheses identifies the EPA accession number of the volume in which the original submission of the study appears. The six-digit accession number follows the symbol "CDL," standing for "Company Data Library." This accession number is in turn followed by an alphabetic suffix which shows the relative position of the study within the volume. For example, within accession number 123456, the first study would be 123456-A; the second, 123456-B; the 26th, 123456-Z; and the 27th, 123456-AA.

OFFICE OF PESTICIDE PROGRAMS
REGISTRATION STANDARD BIBLIOGRAPHY
Citations Considered to be Part of the Data Base Supporting
Registrations Under the Metiram Standard

MRID	CITATION
00030245	Hunter, B.; Barnard, A.V.; Prentice, D.E.; et al. (1979) Metiram Tumorigenicity to Mice in Long Term Dietary Administration. Final rept. (Unpublished study received Apr 10, 1980 under 279-2514; prepared by Huntingdon Research Centre, submitted by FMC Corp., Philadelphia, Pa.; CDL:242192-A, 242193)
00030565	Palmer, A.K.; Simons, R. (1979) Effect of Metiram Technical on Pregnancy of the Rat: BSF 302/79616. (Unpublished study including submitter summary, received Apr 10, 1980 under 279-2514; prepared by Huntingdon Research Centre, submitted by FMC Corp., Philadelphia, Pa.; CDL:242188-A)
00031591	Sortwell, R.J.; Allen, D.G.; Heywood, R.; et al. (1979) Metiram: (Containing 2.2% Ethylenethiourea) Oral Toxicity Study in Rhesus Monkeys: BSF 267/78263. Final Report. (Unpublished study including submitter summary, received Apr 10, 1980 under 279-2514; prepared by Huntingdon Research Centre, submitted by FMC Corp., Philadelphia, Pa.; CDL:242190-A)
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APPENDIX IV

Form Approved. OMB No. 2070-0057. Approval expires 11-30-89.

FIFRA SECTION 3(C)(2)(B) SUMMARY SHEET	EPA REGISTRATION NO.
PRODUCT NAME	
APPLICANT'S NAME	DATE GUIDANCE DOCUMENT ISSUED

With respect to the requirement to submit "generic" data imposed by the FIFRA section 3(C)(2)(B) notice contained in the referenced Guidance Document, I am responding in the following manner:

☐ 1. I will submit data in a timely manner to satisfy the following requirements. If the test procedures I will use deviate from (or are not specified in) the Registration Guidelines or the Protocols contained in the Reports of Expert Groups to the Chemicals Group, OECD Chemicals Testing Programme, I enclose the protocols that I will use:

☐ 2. I have entered into an agreement with one or more other registrants under FIFRA section 3(C)(2)(B)(ii) to satisfy the following data requirements. The tests, and any required protocols, will be submitted to EPA by:

NAME OF OTHER REGISTRANT

☐ 3. I enclose a completed "Certification of Attempt to Enter Into an Agreement with Other Registrants for Development of Data" with respect to the following data requirements:

☐ 4. I request that you amend my registration by deleting the following uses (this option is not available to applicants for new products):

☐ 5. I request voluntary cancellation of the registration of this product. (This option is not available to applicants for new products.)

REGISTRANT'S AUTHORIZED REPRESENTATIVE	SIGNATURE	DATE

EPA Form 8580-1 (10-82)

OMB Approval No. 2070-0057
Expiration Date 11/30/89

GENERIC DATA EXEMPTION STATEMENT

EPA Product Registration Number: ____________________

Registrant's Name and Address: ____

____

As an authorized representative of the registrant of the product identified above, I certify that:

(1) I have read and am familiar with the terms of the Notice from EPA dated ____________ concerning a requirement for submission of "generic" data on the active ingredient ______________________ named under FIFRA Section 3(c)(2)(B).

(2) My firm requests that EPA not suspend the registration of our product, despite our lack of intent to submit the generic data in question, on the grounds that the product contains the active ingredient solely as the result of the incorporation into the product of another product which contains that active ingredient, which is registered under FIFRA Section 3, and which is purchased by us from another producer.

(3) An accurate Confidential Statement of Formula (CSF) for the above-identified product is attached to this statement. That formula statement indicates, by company name, registration number, and product name, the source of the subject active ingredient in my firm's product, or

The CSF dated __________________ on file with EPA is complete, current and accurate and contains the information requested on the current CSF Form 8570-4. The registered source(s) of the above named active ingredient in my product(s) is/are ________________ and their registration number(s) is/are ____________________.

My firm will apply for an amendment to the registration prior to changing the source of the active ingredient in our product.

(4) I understand, and agree on behalf of my firm, that if at any time any portion of this Statement is no longer true, or if my firm fails to comply with the undertakings made in this Statement, my firm's product's registration may be suspended under FIFRA Section 3(c)(2)(B).

(5) I further understand that if my firm is granted a generic data exemption for the product, my firm relies on the efforts of other persons to provide the Agency with the required generic data. If the registrant(s) who have committed to generate and submit the required data fail to take appropriate steps to meet requirements or are no longer in compliance with this Notice's data requirements, the Agency will consider that both they and my firm are not in compliance and will normally initiate proceedings to suspend the registrations of my firm's product(s) and their product(s), unless my firm commits to submit and submits the required data in the specified time frame. I understand that, in such cases, the Agency generally will not grant a time extension for submitting the data.

Registrant's authorized representative: ______________________________
(Signature)

Dated: ____________________ ______________________________
(Typed)

EPA Form 8570-27

OMB Approval No.
2070-0057
Expires 11/30/89

PRODUCT SPECIFIC DATA REPORT

EPA Reg. No. ____________________ Date ____________________

Guidance Document for ______________________________

Registration Guideline No.	Name of Test	Test not required for my product listed above (check below)	I am complying with data requirements by Citing MRID Number or EPA Accession Number	Submitting Data (Attached)	(For EPA Use Only) Accession Numbers Assigned
Sec. 158.120 PRODUCT CHEMISTRY					
61-1	Identity of ingredients				
61-2	Statement of composition				
61-3	Discussion of formation of ingredients				
62-1	Preliminary analysis				
62-2	Certification of limits				
62-3	Analytical methods for enforcement limits				
63-2	Color				
63-3	Physical state				
63-4	Odor				
63-5	Melting point				
63-6	Boiling point				
63-7	Density, bulk-density, or specific gravity				
63-8	Solubility				
63-9	Vapor pressure				
63-10	Dissociation constant				
63-11	Octanol/water partition coefficient				
63-12	pH				

EPA Form 8580-4

OMB Approval No.
2070-0057
Expires 11/30/89

PRODUCT SPECIFIC DATA REPORT (cont'd)

EPA Reg. No. ______________________ Date ______________________

Guidance Document for ______________________

Registration Guideline No.	Name of Test	Test not required for my product listed above (check below)	I am complying with data requirements by		(For EPA Use Only) Accession Numbers Assigned
			Citing MRID Number or EPA Accession Number	Submitting Data (Attached)	
Sec. 158.120 PRODUCT CHEMISTRY (cont'd)					
63-13	Stability				
63-14	Oxidizing/reducing reaction				
63-15	Flammability				
63-16	Explodability				
63-17	Storage stability				
63-18	Viscosity				
63-19	Miscibility				
63-20	Corrosion characteristics				
63-21	Dielectric breakdown voltage				
Sec. 158.135 TOXICOLOGY					
81-1	Acute oral toxicity, rat				
81-2	Acute dermal toxicity, rabbit				
81-3	Acute inhalation, toxicity, rat				
81-4	Primary eye irritation, rabbit				
81-5	Primary dermal irritation				
81-6	Dermal sensitization,				
81-7	Acute Delayed neurotoxicity, hen				

EPA Form 8580-4 (cont'd)

Form Approved. OMB No. 2070-0057. Expires 11-30-89.

CERTIFICATION OF ATTEMPT TO ENTER INTO AN AGREEMENT WITH OTHER REGISTRANTS FOR DEVELOPMENT OF DATA

(To qualify, certify ALL four items)

1. I am duly authorized to represent the following firm(s) who are subject to the requirements of a Notice under FIFRA Section 3(c)(2)(B) contained in a Guidance Document to submit data concerning the active ingredient:

GUIDANCE DOCUMENT DATE

ACTIVE INGREDIENT

NAME OF FIRM	EPA COMPANY NUMBER

(This firm or group of firms is referred to below as "my firm".)

2. My firm is willing to develop and submit the data as required by that Notice, if necessary. However, my firm would prefer to enter into an agreement with one or more other registrants to develop jointly, or to share in the cost of developing, the following required items or data:

3. My firm has offered in writing to enter into such an agreement. Copies of the offers are attached. That offer was irrevocable and included an offer to be bound by an arbitration decision under FIFRA Section 3(c)(2)(B)(iii) if final agreement on all terms could not be reached otherwise. This offer was made to the following firm(s) on the following date(s):

NAME OF FIRM	DATE OF OFFER

However, none of those firm(s) accepted my offer.

4. My firm requests that EPA not suspend the registration(s) of my firm's product(s), if any of the firms named in paragraph (3) above have agreed to submit the data listed in paragraph (2) above in accordance with the Notice. I understand EPA will promptly inform me whether my firm must submit data to avoid suspension of its registration(s) under FIFRA Section 3(c)(2)(B). (This statement does not apply to applicants for new products.) I give EPA permission to disclose this statement upon request.

TYPED NAME	SIGNATURE	DATE

EPA Form 8580-6 (10-82)